THE BRITISH JOURNAL

OF

OPHTHALMOLOGY

JUNE, 1947

COMMUNICATIONS

BINOCULAR VISION * †

BY

DOROTHY CAMPBELL

COVENTRY

ALTHOUGH binocular vision has not so far been made the subject of a Middlemore Lecture—certain allied disorders of vision have been discussed by previous lecturers. It is interesting to find that Mr. Fulford Eales—in 1920—deplored the failure of the Education Authorities to deal adequately with cases of visual deficiency, and particularly with those suffering from squint and amblyopia—while Mr. Haycraft, from his experience in examining recruits in 1943, found the incidence of amblyopia so high, that he too deplored the fact that so many apparently healthy eyes should grow up practically blind. Moreover, he regarded it as " a slur on the care which we oculists devote to our young helpless patients.' The interval between the two lectures was that of a complete generation—and it seems to be in keeping with the

* The Middlemore Lecture delivered at the Birmingham and Midland Eye Hospital, October 25, 1946.

† Received for publication, February 3, 1947.

progressive spirit of Richard Middlemore that we should meet this challenge by a consideration of the physiological factors which maintain binocular vision, and an inquiry as to how we can employ this knowledge—to improve the treatment of cases of abnormal binocular vision.

In presenting my thoughts to you I shall undoubtedly repeat certain familiar facts, but I hope to present them to you in fresh perspective, and to include in them an account of recent observations. The one-eyed man is perhaps not now regarded as an oddity, but he is certainly debarred from many interesting activities, while perfect binocular vision is required for so many occupations in the skilled industrial world of the immediate future, that its lack may determine the fate of a man. The high standards of binocular vision required by the Royal Air Force in this last war led to a mass-enrolment of orthoptic trainers, and the work which they accomplished under the guidance of Air Commodore Livingston in restoring binocular vision to pilots—has I think removed the last barriers which existed between ophthalmic surgeons and orthoptists as to the usefulness of orthoptic training. Indeed, it repeats the challenge to ophthalmic surgeons henceforth to make their proper contribution towards the art of orthoptic training—in order that it shall not run the danger of becoming merely a technical exercise.

The common disorders of binocular vision are well known to you—viz. primary amblyopia—and the allied condition of suppression; strabismus—both paralytic and concomitant—and heterophoria.

Paralytic squint, from its sudden onset and its embarrassing clinical symptoms of double vision and false projection, has been recognised by physicians for many years and has been correctly attributed to a pathological disorder of the cranial nerves or nuclei supplying one or other of the extra-ocular muscles. Concomitant strabismus on the other hand was first regarded as a naturally occurring malposition of one eye—and Dieffenbach in 1840 was the first to attempt its surgical correction. Nevertheless, as long ago as 1743 Buffin had suggested that it was due to unequality of vision between the two eyes—while over a century later Priestley Smith ascribed it to a disturbance of those cortical nervous centres which govern binocular vision.

Up to the beginning of this century—the treatment of squint consisted in a correction of the errors of refraction and cosmetic operation. Claud Worth (1902) was the first to inquire into the significance of the amblyopia which is so often present in a squinting eye—and to treat it by occlusion of the good eye—followed by simple binocular fusion exercises on the amblyoscope.

He believed that a fusion centre existed in the brain which was essential to binocular vision, and was absent or lacking in function in cases of concomitant strabismus. The realisation that a faulty state of binocular vision, *viz.*, heterophoria, can exist without an obvious malposition of the eyes—came later still.

Now if, in the light of our present knowledge, we consider the factors which contribute to the maintenance of perfect binocular vision in man, we find that they are (1) The overlapping of visual fields (2) A strongly developed sense of fusion—and (3) The dominance of macular over peripheral vision.

1. *The Overlap in Visual fields.*—Let us first consider the origin of the overlap in visual fields. Most of us are sufficiently familiar with the phylogenetic development of animals, to know that the eyes were first placed laterally—and then assumed a frontal position. We must also bear in mind the fact that in order of development, conjugate movements of the eyes preceded convergence.

What is known as the nasal half of the retina must originally have been occupied with the receipt of visual stimuli arising *behind* the animal—and with the assumption of the frontal position of the eye—this half of the retina is still occupied with stimuli arising on the outer side of the body. In the first case the reaction of the animal as a whole will be to move away from the object behind it, and in the second case—the animal will be stimulated to make divergent movements of the eyes.

The temporal halves of the retinae, on the other hand, are concerned with the reception of stimuli arising *in front of* the animal. The eyes are mutually attracted instead of being distracted—and there is every incentive for the eyes to converge in an attempt to locate the object more precisely. When the visual axes of the two eyes meet—there is a considerable overlap of the visual fields—which must increase the dominance of the temporal halves of the retinae and strengthen visual attention in the binocular area. A re-arrangement of the optic nerve fibres occurs first in the cats, when instead of there being a total decussation of fibres—the semidecussation with which we are familiar is instituted. It is noteworthy that this anatomical linkage appears to subserve conjugate vision; while the non-decussation of fibres from the temporal halves of the retinae favours binocular vision.

Another interesting anatomical fact is that the power of *convergence* only occurs in animals which possess maculae—*i.e.*, the higher monkeys and man. It is associated with a great development of the brain. Not only are there visual sensory areas in the occipital cortex, but a prefrontal cortical area which is associated

with the acquisition of a wide range of conjugate movement and with convergence. In fact, Kennard (1940) found that destruction of one entire frontal lobe in monkeys had the same effect as destruction of one occipital area, in that the animal did not appear to see objects in a contralateral field of vision. In other words though the sensory stimulus was undoubtedly being received by the animals, appropriate mental reaction was stopped. The *localisation* of an image in a visual field is not then purely a sensory phenomenon but is a sensory-motor response. Holmes has reported two cases in which impairment of the parietal lobe in a patient caused defective spatial orientation—although the visual fields were unimpaired and visual acuity was fair. Riddoch (1935) has pointed out that visual disorientation can occur when the association pathways from the occipital cortex to other parts of the brain are interrupted, the nodal point appearing to be in the region of the supramarginal and angular gyri in the parietal lobe.

This new anatomical evidence is against the theory held by so many ophthalmologists that spatial localisation arises purely from the position of the stimuli which fall on the retinae, or from any exactly recorded pattern of them in the visual sensory cortex.

It is probably the correct conclusion to say that the overlap of visual fields lays the foundation of binocular vision, by concentrating visual attention, so that an object can be located correctly, and that the added powers of convergence and accommodation—serve to make the location precise. The mere overlap of fields does not guarantee the fusion of two images into one. For this a fusion sense appears to be necessary—and is intimately bound up with the sense of projection.

Fusion Sense.—Paralytic squint is the most dramatic instance of a breakdown of fusion. It arises from a motor defect in the extra-ocular muscles, which disturbs the normal position of the visual axes. An attempt has been made to explain the accompanying false projection, also on the basis of a failure of *motor* innervation. It was said to be due to the fact that " When an ocular muscle is weak the increased innervation of the opposing muscle gives an impression of a greater movement of the eye than has really taken place; thus the mind receives the idea that the object is placed farther to one side than it really is, and in an attempt to touch it, the finger may go beyond it." Even so eminent a physiologist as Gowers stated that " We judge of the relation of external objects to each other by the relation of their images on the retina; but we judge of their relation to our own body by the position of the eyeball as indicated to us by *the innervation we give to the ocular muscles.*"

While such an argument might conceivably be true for paralytic

squint, in which defective orientation is partly overcome by secondary deviation of the other eye, and by alteration of head-posture, it is contrary to the facts to interpret all abnormalities of binocular vision as a failure of motor innervation. In concomitant squint the visual axes retain the same relationship to one another over a wide range of conjugate movement—and a *sensory* disturbance occurs in the form of amblyopia or suppression in the majority of cases. Worth explained the onset of suppression as being due to the absence of a fusion centre in the brain—but there is no physiological or anatomical evidence for the existence of such a centre. There is obviously a *sensory-motor* balance in binocular vision—and Franklin (1942) has also emphasised the idea that the functions of fusion, projection and stereopsis depend on this balance—rather than on visual sensations which arise from retinal stimuli alone.

He points out that before the development of the eyes the movements of the body were guided by the impressions received by the lateral sense organs, and that in course of time the eyes took on the same function as the sense organs. We have further evidence of this in the fact that no bird will fly in a fog, because it loses its directional sense, and that a blindfolded pigeon, when loosed from an aeroplane, fails to fly, and drops like a stone.

In animals with laterally placed eyes in which the binocular fields do not overlap, *e.g.*, herbivores and fishes, the animal shows that it can see an object ahead by moving up to it and seizing it. In the carnivores, which have frontally placed eyes—there is a definite correlation between vision and the use of the forelimbs, in the catching and killing of fast-moving prey. The mode of life adopted by the primates, of swinging by hand from branch to branch—requires an exact sense of distance—and projection of an object in space, and we find the anatomical response—of specialisation of the brain, convergence, accommodation and macular vision to which I have already referred.

Thus, in animals, in the fundamental association of body action with visual stimuli, each forelimb is correlated with vision in the *contra*-lateral field. In man, the intimate association of body movement with visual stimuli is well shown in the lack of general co-ordination which often accompanies paralytic strabismus, and is also seen in certain cases of concomitant strabismus when the patient attempts to rely on the amblyopic eye alone.

Franklin has emphasised the fact that fusion and projection in binocular vision are based on *bitemporal* retinal representation —*i.e.*, on the overlapping of nasal fields, but that they are anticipatory in character—and comparable to potential movements.

Let us now consider the third factor which influences binocular vision—*viz.*, ***macular dominance.***

Birds with laterally placed eyes, whose visual axes are set at an angle of 120° or more, have a fovea, so that it would appear that the primary function of the fovea cannot be one of fusion. Nocturnal birds of prey, with frontally placed eyes, have two foveae in each eye.

The macular fibres in man are distributed over an area which extends for approximately 20° in a horizontal direction on either

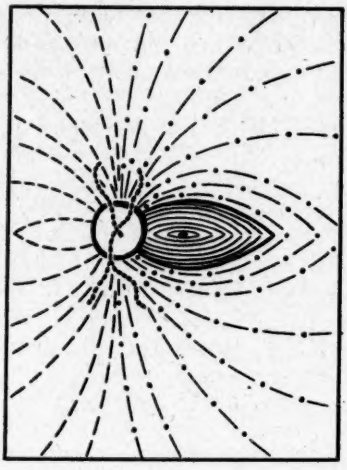

FIG. 1.

The course of the visual fibres of the retina.

side of the macula and embraces the blind spot on the nasal side (Fig. 1). Vertically the area extends for about 3° above and below the macula. Visual acuity within this central area rises from 6/60 at the periphery to 6/6 at the fovea (Fig. 2).

On account of the superiority which this visual acuity and pattern vision has conferred on man—we are apt to consider that it dominates over the more primitive visual function of fusion. It is important to remember in this respect, that bitemporal retinal representation persists throughout the central area of the retina —and the overlap of the visual fields must be as shown in Figs. 3 and 4. One would expect to find, as is indeed the case, that fusion is very strong in the paramacular area, and it decreases peripherally.

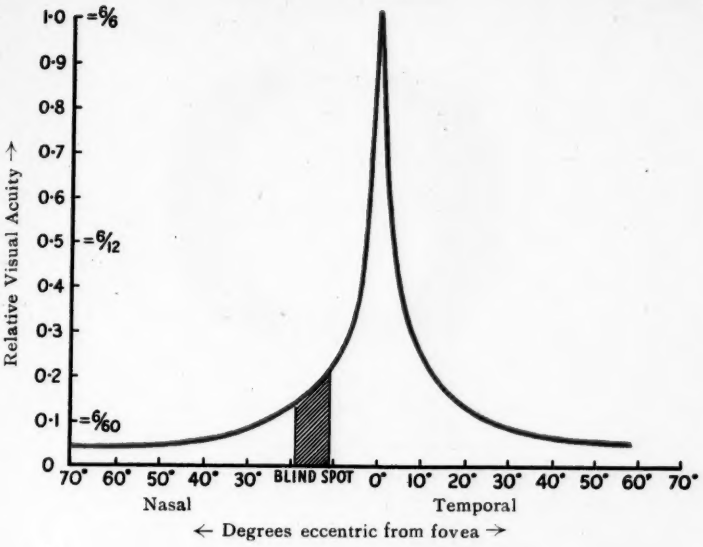

FIG. 2.

The regional variation of visual acuity (after Wertheim).

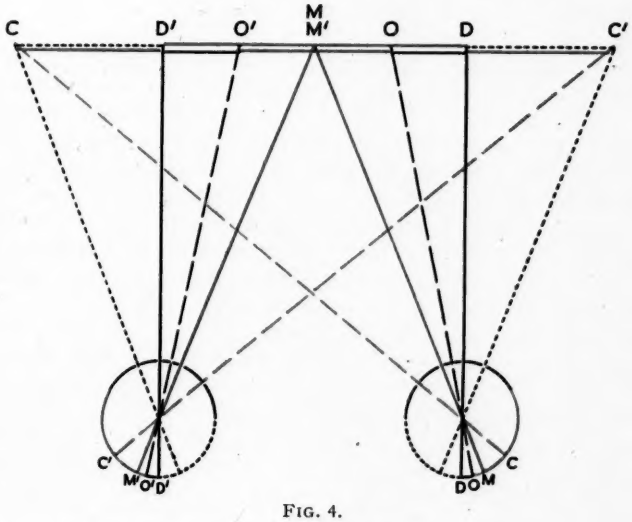

FIG. 4.

Overlap of visual fields in binocular fixation (central area).

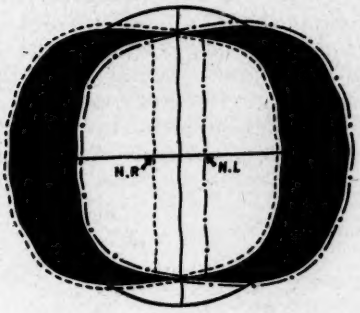

FIG. 3.

The overlap of visual fields in man.

□ *Binocular vision.* ■ *Monocular vision.*

n.r. = nasal limit for "central field," right eye. n.l. = nasal limit for "central field," left eye.

The maintenance of perfect binocular vision must depend on a bilateral harmony within the central area, of the two mechanisms of pattern vision and fusion. This probably occurs only in a minority of individuals, since the possibilities of the breakdown of so fine an adjustment are so many. It has in fact been said (Bielchowsky, 1937) that only about 20 per cent. of individuals with good binocular vision are really orthophoric, and recent observers have found evidence of a continual competition between foveal vision and the fusional processes occurring in the area immediately outside the fovea.

In certain pathological conditions there is a surprising maintenance of binocular vision; *e.g.*, subjects suffering from retinitis pigmentosa, in which the function of the peripheral retina is entirely lacking, can still maintain binocular vision when only a small central field remains and their visual acuity is very low. Conversely subjects with bilateral macular degeneration or disease also may retain some degree of fusion. A study of binocular vision in conditions of partial loss of visual field, would, I think, elucidate the functional balance between the peripheral and central areas of the retina, still further.

In a series of tests on another aspect of this problem, which have been made recently at this hospital, we have found that good binocular vision persists in the dark adapted eye—even when the illumination of the test object is so low as to favour rod, rather than cone, vision. The subjective angle tends to become convergent; there is a general tendency to giddiness, and colours are

suppressed. Some degree of stereopsis persists even when visual acuity is greatly diminished,

The *physiological* abnormalities of binocular vision (see Table 1) may be tabulated as shown. We find all degrees of variation, from a complete competition between the eyes, as in alternating strabismus, down to total suppression of central vision in one eye. Thus at each end of the scale—vision becomes uniocular rather than binocular. In the intermediate grades some attempt

TABLE I

Physiological Abnormalities of Binocular Vision

1. Alternating strabismus	...	Uniocular vision
2. Congenital nystagmus	...	Usually some degree of binocular vision
3. Heterophoria Low degrees of concomitant strabismus False associated fixation	...	Abnormal binocular vision due to rivalry within the "central" area of the retina
4. Large degrees of concomitant strabismus (*a*) with, and (*b*) without suppression	...	Abnormal function in both "central" and peripheral retina
5. Advanced suppression with loss of central fixation	...	Peripheral function only in affected eye; binocular vision poor or absent

at binocular vision is made. In by far the majority of cases this is accomplished by the partial suppression of pattern vision—which has been abundantly proved to be a mental process of ignoring the image from one eye. In others, although visual acuity is full, foveal fixation gives way in order that extra-foveal fusion can be maintained; or competition is avoided by establishment of a false macula—in the condition we recognise as false associated fixation.

When the central area of one eye is very defective—abnormalities of orientation occur. The onset or non-occurrence of strabismus is, I believe, determined at its onset by the initial level of visual acuity in the eye affected. By referring again to the curve for visual acuity (Fig. 2) we are reminded that the central area includes the blind spot, so that " the margin of escape " is only 10° on the nasal side of the macula—and any failure in this region will favour the development of a convergent strabismus.

You will notice that I have so far avoided making any reference to the subject of retinal correspondence. It has long been considered that stereopsis was due to the stimulation of corresponding points on the retina, and to an exact reinterpretation of such stimuli in the visual sensory cortex. I have already shown that this is not true in the case of the primitive fusional mechanisms—and recent work has shown that it is too precise a theory to be applied even to foveal fixation.

McAllister (1905), Dodge (1907) and Clark (1936) have shown that in normal binocular vision an area of 1—1·5° from the fovea

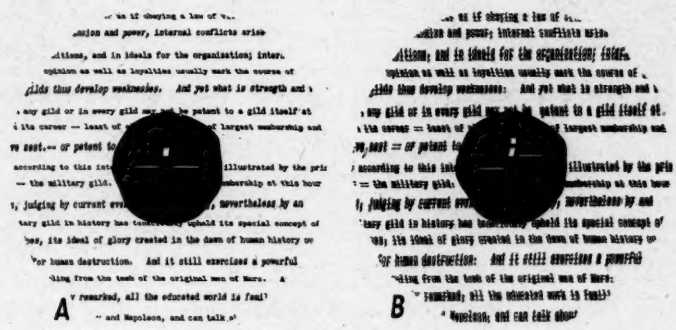

FIG. 5.

Diagram showing the doubling of a centrally fixated object (1° square) by displacement of peripheral images (print), A, superimposed, B, displaced (Burian, 1939).

can be used for fixation—and with a disparity of 2—4° horizontally and 2° vertically in either direction an object will still be reported as single. Burian (1939) made a further discovery that peripheral retinal stimuli, if displaced, by as small an interval as 0·25°, will break the fusion of images situated on corresponding areas of the macular region, and no matter how hard the observer tries he is unable to maintain central fusion in the presence of displaced peripheral stimuli (Fig. 5). Burian made these tests within an area of 12° round about the macula. Stimulation of smaller areas of $\frac{1}{2}$—1° at a distance of 12° from the face caused noticeable fusional movements of the eyes. Burian concluded from his observations that there must be a large number of individuals who will never be able to fuse central and paracentral images simultaneously; some in fact maintain a rapid small alternation.

He later (1941) examined 75 cases of concomitant strabismus with less than 12° strabismus and full visual acuity. He found that the eyes performed small fusional movements in order to maintain

binocular vision, and that patients who had no foveal suppression, showed a small degree of suppression in the paramacular area. Paramacular fusion could only be maintained at the expense of foveal fixation being out of alignment. The exceptions were (*a*) alternation, due to suppression of all the images of each retina

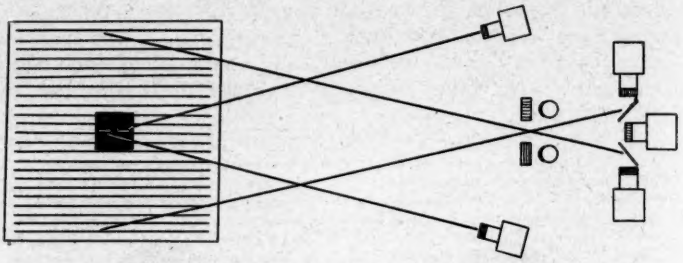

FIG. 6.

Peripheral fusion (of superimposed line pattern) and foveal test lines on a level. Images seen as above, *i.e.*, unchanged by (*a*) Patient with normal binocular vision. (*b*) Patient with strabismus with anomalous correspondence adapted to the angle of squint (Burian, 1941).

in turn; (*b*) The presence of a false macula, which supported all the attributes of binocular vision except stereopsis (Fig. 6). His methods of experiment were both accurate and ingenious.

A comparison of the average number of eye-movements made per second, while the eyes "fixed" isolated points and points in context. (Clark), 1936.

(By kind permission of Professor Clark, *Amer. Inst. Psychol.*, 1939)

	Horizontal component		Vertical component	
	R. E.	L. E.	R. E.	L. E.
Isolated point A	7·55	7·01	4·11	6·20
Point A in context ... (*i.e.* viewed in a picture)	6·88	7·59	3·88	6·39
Isolated point B	6·98	6·66	4·28	5·53
Point B in context ...	7·08	6·55	3·83	5·44

FIG. 7.

The improvement of the camera has made it possible to make objective records of the movements of the eyes—rather than having to rely entirely on subjective phenomena.

Judd (1907) was the first to photograph the movements of the eyes in convergence and divergence. He found that as they viewed two fixed points in space, the eyes of some subjects made conjugate movements prior to convergence, while others moved one eye faster than the other. In short there was no exactitude of movement in fixation. The same observation was made by Clark (1936) who from an analysis of over 3,000 photographic records found that the quality and quantity of the movements was the same for stereoscopic vision, as in the fixation of an isolated point (Fig. 7). The eyes made an average of 8 movements per second, but one eye moved more often than the other (Fig. 8). Clark

Average number of movements per second made by the eyes fixing points in a Stereogram (Clark).

(By kind permission of Professor Clark, *Amer. Inst. Psychol.*, 1939)

	Fixating					Fixating				
	Near Point		Far Point			Near Point		Far Point	
Subject	R.	L.	R.	L.	Subject	R.	L.	R.	L.
1	5·9	9·9	10·2	13·8	9	5·3	8·1	3·3	7·0
2	5·1	5·8	6·0	6·2	10	4·1	7·0	11·9	9·2
3	11·8	13·7	15·9	14·1	11	9·0	6·8	8·2	7·2
4	7·7	9·2	9·1	9·9	12	5·8	2·4	3·1	3·8
5	7·1	9·8	8·9	12·0	13	8·3	6·9	8·8	10·2
6	9·8	7·2	8·7	10·9	14	11·1	9·9	10·0	9·1
7	9·0	11·7	5·9	5·8	15	5·2	7·1	5·1	5·2
8	7·9	8·3	6·2	10·8	16	—	—	8·8	11·8

FIG. 8.

concluded that clear visual perception can only occur at the movement of fixation—and in the interval visual acuity must be diminished. Obviously then, visual perception must constantly be both binocular and monocular, and shift from one eye to another. He suggests that the highest grade of binocular vision must therefore depend on the organisation and unification of minimal changes—rather than on the stimulation of specific geometrical or corresponding points on the retina. He believes that stereopsis must be made up of a rapid comparison of uniocular impressions, and in this he is supported by Litinski (1939) who found that in 72·5 per cent. of normal subjects which he examined, the uniocular perception of solidity was equal to the binocular perception. Verhoeff too supports the theory that binocular vision occurs by uniocular replacement—rather than by simultaneous vision of the two eyes. He believes too, that while one eye is occupied with the observations of one portion of space, the other eye is suppressed in this region only—so that the two eyes divide between each other the entire field of vision in an ever-changing mosaic of small uniocular part-fields. Verhoeff's conclusions were based on subjective phenomena—but the objective experiments of Burian and Clark go far to substantiate them. In an analysis of amblyopia which I made earlier this year (1946) I arrived at the same conclusion, *viz.*, that binocular vision depends on some form of physiological replacement. It is certainly the only theory which explains all the abnormalities of binocular vision, particularly those which arise from functional disorders of the central area of the retina. Thus Hering's theory which states that in binocular vision the image is projected along the visual axis of a hypothetical cyclopian eye—midway between the two eyes—appears obsolete. The elaboration of this theory to explain stereopsis as due to the simultaneous stimulation of corresponding and disparate points of the retina also appears to me to be impossible. I was surprised to find that the latest definition of stereoscopic vision which has been given to orthoptic students is " the ability to fuse images falling on *slightly* disparate points of the retina." It is difficult to reconcile this with any theory of binocular vision.

In conclusion, I shall attempt to apply these newer concepts of binocular vision to the practice of orthoptics.

The young child resembles the animal in its development, and its early years are spent in learning to correlate its body reactions with visual stimuli.

I cannot resist quoting from Richard Middlemore's " Treatise on diseases of the eye," certain passages in which he lays stress on the very early onset of strabismus (1835).

In early life, children are sometimes placed very injudiciously in their cradle, or they are, perhaps, very generally carried in one and the same position, so that the light gains more frequent and complete access to one organ than to the other, in consequence of which, that eye which is most familiarized with the influence of the luminous rays, is more readily stimulated by them, and the other is rendered, in a corresponding degree, the more insensible to them. Again, sometimes the infant's cap is ornamented with a long and partly coloured border, so that it readily attracts the child's attention, and he is continually turning the eyes towards it, as he lies in the cradle. In the same way a small spot, naevus, or tumour upon the nose, may produce squinting by disposing the child to look at it very intently, and he is inclined to make great and repeated efforts to turn the eyes towards the object of attention, because it is not distinctly seen. Of these two causes of infantile strabismus, the former will cause strabismus divergens, and the latter strabismus convergens.

7.—Imitation is certainly a cause of strabismus; parents will often tell their medical attendant that their child did not squint when he left home for school, but, on his return, the strabismus was complete; and the child will probably mention that many of his school-fellows also squinted, because they were frequently mocking or imitating each other. No cause of strabismus is more satisfactorily made out than this.

8.—Sometimes one of the eyes happens to be inflamed in early life, and it is carefully bound up, until its visual powers become impaired from prolonged repose from its natural actions and the long absence of its natural stimulus; such an eye will be liable to be affected with strabismus, unless, which is very improbable, its retina should again recover its sensibility. In other instances both eyes may, perhaps, be slightly inflamed, and the surgeon may tell the parents of the child to protect them from the influence of bright light, and they will bind them up, as they conceive, very carefully, in order to fulfil what they presume to be the Doctor's wish the better, and in this way the patient will be totally deprived of his sight during the continuance of the ophthalmia, at least, according to the parent's intention; but children do not like this deprivation, and therefore so change the situation of the bandage, as to see either upwards or downwards, and, in this way, acquire a habit of squinting. Many of the worst cases of strabismus of both eyes, which it has fallen to my lot to notice, have been so caused.

It is certainly a pity to lose the early years as a time for training. The sense of fusion can only be properly developed if the two eyes are used equally. Visual acuity should be brought to a maximum by ordinary glasses at as early an age as possible—and occlusion should not be left, as it so often is in the hospital child, until the age of 5 (Fig. 9). It can be employed much earlier—or perhaps a better method is the use of atropine drops in the good eye, in order to bring about fixation in the squinting eye. I have never known this method to cause false associated fixation to develop—and it has the advantage that it can be started in infancy—and that the child continues to exercise some degree of binocular vision—whereas occlusion cut out any stimulus to fusion. There is a good deal of evidence that the amblyopic eye supplies a spatial background to the good eye, and this must be the explanation as to why quite a number of adult amblyopes have straight eyes and a certain degree of fusion.

The next stage of fusion training is not usually started until about the age of 6, because the child cannot understand the synoptophore and has not sufficient mental application. I think more use might be made of the toy games in the interim.

The development of visual acuity in the young child, following treatment. (Campbell, 1946)

	Treatment under 5 years				Treatment over 5 years	
	Group A		Group B		Group C	
Vision	Before	After	Before	After	Before	After
	per cent.	per. cent.	per cent.	per cent.	per cent.	per cent.
<6/60 ...	15	0	27	0	10	5·2
6/60–6/24	28	2·4	38	2·2	43	5·2
6/18–6/9	57	9·6	35	20·0	47	12·0
6/6 ...	40	88·0	0	77·8	0	77·6
No. of cases	47	Treated by atropine drops followed by occlusion	45	Treated by occlusion only	58	Treated by occlusion only

FIG. 9.

Again fusion training is delayed until vision is nearly equal in both eyes, but Swan and Laughlin (1944) have recently advocated it, when the vision in one eye is still much below standard. They state that provided that the target is large enough to correspond with the degree of vision, or to avoid the central scotoma—peripheral fusion can be established and appears to assist in the development of central vision.

Cases of heterophoria excluding large degrees of height, seem to improve adequately on duction exercises. I have found that quite a number, *e.g.*, 42 out of 78 cases, show a small degree of suppression—which is frequently alternating and appears only in the fixing eye. This suppression is no obstacle to their cure—because of the strong fusion sense which is always present.

False associated fixation presents one of the most difficult problems of training. In a group of 74 cases I found only one cure. The data showed that they all had, or regained, equal vision in both eyes—and showed a macular dominance, but with very little power of fusion. The subjective angle in every case except one

was under 10°—*i.e.*, it corresponded to the retinal area between the disc and the macula, while in one case only the angle was 19°—*i.e.*, immediately to the nasal side of the disc.

It has been suggested that in these cases operation should precede orthoptic training, but what is needed appears to be some form of training to develop peripheral fusion and by the use of large images, rather than to attempt to change macular vision from " false " to " true," a process which takes an exceedingly long time and has such strikingly poor results. Events might prove that the resumption of peripheral fusion would lessen the disparity in central fixation.

Finally, although the standard set by the British Orthoptic Council for a cure is quite commendable, I think it is far too high for every day purposes.

Costenbader (1945) in an analysis of the causes of failure in the treatment of squint, has suggested 4 grades of cure :—

(1) British Standard (1939). Straight eyes, normal vergences—good fusion and stereopsis.

(2) Good fusion and stereopsis, but varying from fusion to diplopia with Worth's test, and inconstant ability to bar read.

(3) Fair fusion—fair vision and a small degree of residual strabismus.

(4) Cosmetic cure—no fusion—a small degree of residual strabismus.

You will notice that fusion with convergence is only achieved in the highest degree of binocular vision. Stutterheim (1940) has advocated a new form of training based solely on convergence exercises. He starts, as it were, at the other end of the scale —and states that amblyopia may persist for a considerable time *after* the squint has been cured. Although he pours scorn on the recognised methods of orthoptic training, his book is worth reading, by way of contrast.

I have not attempted to analyse the surgical treatment of binocular abnormalities, but I think you will agree that good surgical results depend more on the moment chosen for operation, rather than on the exact adjustment of the angle of squint. I must end my discourse with an apology for the inadequate analysis of the subject of binocular vision, which I have been able to make. Perhaps some Middlemore lecturer of the future will be able to give us more advanced information. The present jig-saw of facts will then be transformed into a complete picture.

REFERENCES

BIELCHOWSKY, A. (1937).—The etiology of squint. *Amer. Jl. Ophthal.*, Vol. XX, p. 478.

BURIAN, H. M. (1939).—Fusional movements. *Arch. Ophthal.*, Vol. XXI, p. 486.

——— (1941).—Fusional movements in permanent strabismus. A study of the role of the central and peripheral regions in the act of binocular vision in squint. *Amer. Arch. Ophthal.*, Vol. XXVI, p. 626.

CAMPBELL, D. A. (1946).—Primary amblyopia. *Trans. Ophthal. Soc. U.K.*

CLARK, B. (1936).—*An eye movement study of stereoscopic vision.* *Amer. Jl. Psychol.*, Vol. XLVIII, p. 82.

COSTENBADER, F. D. (1945).—Causes of failure in the treatment of squint. *Amer. Jl. Ophthal.*, Vol. XXVIII, p. 1123.

DODGE, R. (1907).—An experimental study of visual fixation. *Psychol. Monogr.*, 1.

EALES, FULFORD W. H. (1920).—Some aspects of convergent strabismus. Middlemore Lecture.

FRANKLIN, I. (1942).—Fusion projection and stereopsis. *Amer. Jl. Ophthal.*, Vol. XXV, p. 1316.

HAYCRAFT, G. H. (1943).—Amblyopia ex anopsia (with special reference to recruitment for the armed forces). Middlemore Lecture.

HERING (1863).—*See* DUKE-ELDER, *Text-book of Ophthalmology, Vol. I, p. 1062.*

JUDD, C. H. (1907).—Photographic records of convergence and divergence. *Psychol. Monogr., pp. 6, 370.*

KENNARD, M. A. (1940).—Alteration in response to visual stimuli following lesions of frontal lobe in monkeys. *Arch. Neurol. and Psychiat.*, Vol. XLI, p. 1153.

LITINSKI, G. A. (1939).

MCALLISTER (1905).—The fixation of points in the visual field. *Psychol. Monogr.*, pp. 7, 17.

RIDDOCH, G. (1935).—Visual disorientation in homonymous half fields. *Brain*, Vol. LVIII, p. 376.

STUTTERHEIM, N. A. (1940).—Squint and convergence. H. K. Lewis & Co., Ltd., London.

SWAN, K. C. and LAUGHLIN, E. (1944).—*Binocular orthoptic training for amblyopic patients.* *Amer. Arch. Ophthal.*, Vol. XXXII, p. 302.

WORTH, C. (1902).—Squint, its causes, pathology and treatment. Sixth edition, 1929.

VERHOEFF, F. H. (1935).—A new theory of binocular vision. *Arch. Ophthal.*, Vol. XIV, p. 419.

MIDDLEMORE, R. (1835).—A treatise on the diseases of the eye.

THE REGENERATION OF WOUNDS OF EXTERNAL *MEMBRANE OF THE EYE IN THE LIGHT OF* NEW PATHOLOGICO-ANATOMICAL RESULTS*†

BY

Professor E. TH. LEVKOIEVA

MOSCOW

PART I

Introduction

WHILE paying due consideration to the questions raised by *ophthalmic surgery during* the last war, we have to point out that insufficient attention was paid to the conditions at the moment of

* From the pathological-histological Department of the Central Institute of Ophthalmology, named after Helmholtz Director, Professor Kolen'; in charge of pathological-histological department, Professor Levkoieva. Translated by Dr. N. Pines. † Received for publication, November, 1946.

the wounding, and the further fate of the eye very often depends on them. In the Russian ophthalmological literature during the last war a criticism of the principles of the management of perforating eye-wounds was started (Levkoieva, Braunstein, Jenkin-Harkavy). From that point of view it is important to study (pathologico-anatomically), the eyes enucleated after trauma. We have studied during many years a large number of such eyes (about 6,000 altogether) enucleated as a result of different kinds of trauma; the study of war wounds during the " Patriotic War "—all these researches lead us to the conclusion that at present the first surgical measures do not guarantee a good healing of the wound. The pathologico-anatomical analysis shows that the wounds are left in an unsatisfactory condition, and this by itself, quite independently of other causes, may lead to fatal complications in the wounded eye.

The fact that those eyes had to be enucleated does not diminish the value of our material in forming those or other principal questions; first of all because the necessity of enucleation does not prove the extraordinary degree of the trauma itself. Because the eye is so small, forming a compact whole, relatively isolated, it is possible to study in it the causes and consequences of the changes better than in any other pathologico-anatomical object. This study brings us to the conclusion that parallel to the severe trauma, that certainly destroys many eyes, in a very important percentage of the enucleated eyes the *fons et origo mali* was not a severe trauma, but certain complications were the leading factors in the disastrous result. This is why the consequence becomes the cause, and this is why it is important to study and to fight it.

The fact of the enucleation does not exclude the fault of the ophthalmic surgeon, as far as the unsatisfactory state of the eye-wound is concerned; he struggles a long time before he decides on enucleation, even in large scale trauma, while the microscopical examination shows that his efforts were powerless and frustrated in cases, where from the beginning the right measures were not taken to close the wound. What result can show later the symptomatic and reabsorbing therapy, if under the well-formed scar of the conjunctiva the edges of the scleral wound are turned inwards or lie one on top of the other or the wound is still not closed? These conditions are the cause of constant irritation, reactive inflammation of the anterior part of the uvea and a source of haemorrhage in the wounded eye.

Following this reasoning and considering the importance of the correct approach by an ophthalmic surgeon to a fresh wound of the eye we analysed in our work the surgical principles up to date.

In the first instance we examined the question of infection in the eye injury. There are no serious bacteriological researches of this

point and we had to study it on the large pathologico-anatomical material at our disposal. We thought the solution of this problem to be so urgent, because at present the question of infection is a basic one in all surgical measures for the wounded eye. And after analysing the present methods of healing of eye wounds from this point of view, we came to the conclusion that the ophthalmic surgeon approaches this problem exactly like a general surgeon does to any kind of wound, and we started to search for a basis of rational therapy for eye wounds.

Finally we have examined a *sui generis* regenerative process of the external membranes of the wounded eye of considerable theoretical and tremendous practical importance. This factor at present is not appreciated and even not recognised by the clinician in his therapeutic or surgical measures. This is why we are going to characterise the essence and importance of those changes during the healing up of eye wounds. At the same time we have touched on the sore points of traumatic iridocyclitis—a general term that covers in clinical practice a whole range of changes in the wounded eye.

Accordingly the present paper comprises the following sections:—

(1) Clinical and anatomical approach to perforating wounds of the eye.

(2) A review of the methods of closing eye wounds.

(3) The regenerative process of the external membranes of the eye.

(4) Classification of eye injuries.

(1) Clinical and anatomical approach to perforating wounds of the eye. The most important factor which decides the fate of the eye is the exogenous putrifying infection that penetrates the eye at the moment of trauma, and, secondly, sympathetic ophthalmia. With the trauma as a background these two items decide the fate of the eye. The fear of infection defines the surgical measures when treating a fresh eye wound and the fear of sympathetic ophthalmia haunts the clinician all the time while healing is going on.

The infection is the foremost in the primary treatment of the eye wound. Some surgeons prefer to leave unsutured large wounds of the cornea and sclera, fearing the infection that penetrated the eye at the moment of trauma, and the same consideration of infection decides the method of operation when dealing with a fresh wound. The majority prefer to cover the wound of the anterior eye segment with a flap of conjunctiva (Kuhnt's method), and lately this operation completely replaced the suturing of the eye membranes

themselves with a close fixation of the edges of the wound—a method proposed more than 100 years ago and, according to the *literature, beneficial in a* whole range of major wounds.

In the further progress of the traumatic process the fear of *sympathetic ophthalmia is so* much in the centre of the surgeon's attention that it exceeds all other possibilities impressing itself *clinically (precipitates,* ciliary pains, hypotony) and leading to the decision to enucleate. The last resolution the surgeon accepts *after long* deliberation but usually with the same diagnosis of traumatic iridocyclitis, *i.e.*, he does not think of infection and does *not diagnose* " endophthalmitis," but he fears sympathetic ophthalmia and therefore enucleates the eye.

First of all let us state that the clinician has an exaggerated idea about traumatic infection—the kind of infection that is *labelled* " *endophthalmitis* "—this kind of infection is also covering the reactive inflammation of the alteration phenomena, toxic *inflammation, due to the* presence of the foreign body, endophthalmitis phakogenica.

As a result the clinically diagnosed infection and the diagnosis of endophthalmitis very frequently are disproved by microscopical *examination, and even an abscess* of the vitreous proves often the result not of an infection, but of the previously described causes, *like a foreign body, or endophthalmitis* phakogenica—both of them not only clinically but also morphologically are very similar with some variations that only experienced pathologico-anatomists can recognise.

These are the results of our investigation about frequency of infection in the pathologico-anatomical material.

In 1941, among 263 enucleated traumatised eyes examined in the pathologico-histological department of Helmholtz's Institute in 56 (21 per cent.) we found endophthalmitis without any attempt to differentiate between the causes of it, as mentioned previously. In 1942, among 36 enucleated traumatised eyes we tried to separate the infective endophthalmitis and found it in 24 eyes (6·5 per cent.); in 1943, for 279 eyes, in 7·3 per cent. In 412 eyes enucleated as a result of air raids on Moscow we saw two cases of infection—4·7 per cent. In war wounds the percentage of infection is still lower—among 124 enucleated eyes—in 3·2 per cent. Altogether, for 779 eyes (including 1941) the percentage of infective endophthalmitis, according to pathologico-anatomical examinations, was approximately 5·7 per cent.

Dr. Jenkin-Harkavy on a smaller material of 100 enucleated eyes saw 12 per cent. infected (*Vest Ophtal.*, Vol. XXIII).

Prof. Braunstein also thinks that the prevalent opinion about the frequency of infection in eye trauma is exaggerated.

The microscopical study of wounded eyes leads us to a different opinion—you must not approach the perforating eye wound with ordinary general surgical methods. The ophthalmic surgeon must realise that the eye is a complicated closed system with very superficial correlation of the internal parts, where a small concussion, minimal processes of exudation or haemorrhage could be the primary cause of destruction of the eye. With wounds of the external membranes (cornea and sclera), because they are the capsule of the eye and so influence its form, all this happens more readily. With more or less considerable wounds of this capsule, especially with wide separation of the edges of the wound, this alone on purely mechanical grounds causes a disturbance of correlation within this delicate viscus with all the following consequences. When you study such eyes enucleated after a trauma and see widely separated edges of the wound wrongly healed up, with badly adapted edges, you are able to understand the colossal impairment, changes, disturbances of blood-circulation—all of them frequently accompanying the regenerative process of the eye and quite independent of the results of the trauma itself.

The primary task of the surgeon is to restore immediately after the trauma the disturbed correlation of the tissues in the eyes of a more or less large wound (more than 5—7 mm.), if, of course, he has the slightest hope of preserving the function of the eye and if he does not decide on immediate enucleation—an indication really present in a few cases, with a complete destruction and prolapse of all interior membranes of the eye.

We have analysed from this point of view 120 cases of war wounds. In all cases, where the wounds were in an unsatisfactory state, in 100 per cent. we saw a disturbance of blood circulation and very often a direct connection of the haemorrhages with the hole of the wound. Fresh repeated haemorrhages, occurring very late after the injury, are the proof of constant irritation resulting from a non-closed or badly closed wound.

And so the state of the wound is a factor of primary importance for a favourable healing result. Whatsoever happens later about the infection showing itself, we cannot decide in the beginning. If there is a foreign body—the closing of the eye wound cannot be delayed. Obviously, if an electromagnet is available we will first extract the foreign body and only after that will we close the wound. But if the electromagnet is not available—we must first of all close the wound properly and the foreign body will be extracted at the first opportunity later on. With a widely used diascleral approach the surgical incision very often does not correspond to the wound, and if we do not close the traumatic wound immediately we may be too late, even with a successful extraction of the

foreign body. In cases of added infection we have no reason at all to prove that leaving the wound open gives more chances for recovery and because of that to neglect to close the wound immediately.

As a résumé, we have to point out that in more or less large perforating wounds of the eye we have to consider not only the question of infection, but the whole clinical-anatomical position—that dictates an immediate reconstruction of the disturbed correlation on the anatomy of the eye, following the trauma.

Conclusion.—The healing process and the fate of the perforated eye depends chiefly on the primary surgical treatment.

(2) Review of the surgical methods of closing eye wounds. In the last war the question of closing eye wounds became of first importance.

It seems that it is worth while to re-examine the approach of the ophthalmic surgeon to wounds of the eye and its different membranes in the view of better results in healing because many sides of this question are still not decided.

From the point of view of the previously described anatomical factor the first task of the military or civilian surgeon is the earliest and best closure of the wound of the external membranes. What are the best methods in different wounds? They are only two—suturing of the sclera and cornea and the plastic of the conjunctiva bulbi by the method of Kuhnt. But we have to mention here that there exists a school of surgeons, who not only do not operate even on large wounds, but even do not excise the prolapsed membranes—and those membranes for certain do not allow the wound to heal up, as witnessed by unsuccessful operations with their incarceration in the scar, usually ending with enucleation. The fact is that in the great percentage of unsuccessful operations the bad result is due exactly to the membranes, caught in the scar and impeding the good healing up of the wound. The reason for this school's idea is the fear of infection that penetrated the eye with the trauma (Strachoff and his school). The partisans of this school do not enucleate the eye for a long time, even with very large wounds, and apply therapeutic measures, hoping eventually that large wounds of the cornea and sclera can heal up by themselves without any surgical interference. The microscopical examination of such enucleated eyes shows that as a rule spontaneous healing does not occur, and the wounds are in a highly dangerous state even without talking about the prolapsed membranes.

Let us now review the methods of closing the eye wounds. The simplest and most successful method—that of Baroti, published more than 100 years ago—is to suture the sclera, the edges of which usually are widely separated, because the sclera has a peculiar

morphological structure (plenty of elastic fibres, and moreover the muscles attached to it usually contract). As a result of the sutures the edges of the scleral wound are joined together, and are fixed in a proper position, thus having the necessary conditions for healing up. Dieffenbach sutured the cornea in 1847. In Russia, Ginsbur was the first to apply sutures to the sclera. The old Russian ophthalmic surgeons (Odinzof, Strachoff, Auerbach, Blagovechensky) previously always applied sutures in the wounds of the external membranes, if the wounds were larger than 5 mm. or were yawning. Varshofsky was a great partisan of suturing, and described cases when the sight later on was 0·3—0·5, although in the beginning it was nil (amaurosis). But now the suturing of the wounds in Russia and, according to the literature abroad is done much more rarely. This method not only did not become a usual one, but its results are described and recommended as rarities. H. K. Müller, in 1945, in his book, "Ophthalmologische Operationslehre," advances the importance of surgical closure of perforating wounds and recommends suturing (but not through the whole thickness of the sclera or cornea).

The second school thinks that it is advisable to suture only the conjunctiva, leaving the wound of the sclera alone. The method of conjunctival plastic by Kuhnt has lately become very popular and is widely employed in all kinds and dimensions of wounds, but unfortunately without the special individualisation demanded by Kuhnt himself. With a conjunctival flap the surgeon likes to cover even large wounds of the cornea and sclera, hoping that in this way the edges of the wound will remain joined. He is usually wrong.

The best method of controlling the success of this or other methods is the microscopical examination.

In 1941—1942, on the material supplied by air raids on Moscow, we could study the state of the wounds in severe injuries in 42 enucleated eyes; in 13 of them Kuhnt's method was applied, and the rest were treated conservatively. Moreover, we analysed in detail a large amount of material in 1941 in 263 enucleated eyes, where 63 eyes were operated on by Kuhnt's method, and in the rest no surgical measures were applied.

Let us speak first of all of the conjunctiva when discussing Kuhnt's method. Its usual rôle is described as follows:—

It protects the eye against secondary infection, and it is a very good corneo-scleral plastic material. But both opinions are wrong, as discussed above; even the danger of primary infection is not great, and that of a secondary infection still less so. And the importance of the conjunctiva as a good plastic material for formation of scars on the cornea or sclera is contradicted by actual facts,

because, according to the present literature, the regeneration of these membranes is produced by their local elements, and the conjunctiva does not form a scar.

The part taken by the conjunctiva, according to our material, is as follows:—

In 10 per cent. it still covered the wound. But much more often one can see only its débris present and then from time to time, hardly joined with the wound and therefore having neither a prophylactic nor a joining action. And even in cases where it is present it only covers the wound; it does not penetrate deeper and does not take part in the regeneration. The regenerative process of the external membranes of the eye goes on independently; the newly formed tissue, often filling up the wound and penetrating into the anterior chamber, sometimes goes even under the conjunctiva, but *vice versa* one cannot see any elements of the conjunctiva in the scar. But after Kuhnt's operation in the majority of cases epithelium is present in the scar; it proliferates largely and penetrates inside the wound, covering parts of the edges of the wound and growing to a considerable depth.

And so we have to reckon when performing this operation with the participation of the epithelium in forming cystoid scars, fistulae and real cysts; one sees all those things very frequently, not even mentioning rarer possibilities, such as the growing of the epithelium into the anterior chamber and encapsulating it with all its important consequences.

In all cases of Kuhnt's operation the prolapsed membranes were excised. This first and important step gave good results according to microscopical examination. In the majority of cases the membranes were thoroughly excised and were absent from the wound. But unfortunately the same good opinion cannot be given for the healing up of the wound.

And here we have to differentiate between large yawning wounds and small ones that clinically healed up with a small scar. In the first case the widely separated edges of the wound show that the flap of the conjunctiva cannot keep them joined. Even clinically we notice that on the second or third day after the operation the conjunctiva is off the surface of the wound, or the edges of the wound are not covered with the conjunctiva. Microscopically we often see that the edges of the wound were not joined together and the space between is filled up by newly formed regenerative tissue, or is simply yawning, and the edges may be already covered by epithelium.

In all these cases all the complications were present that are usually caused by non-restitution of the anatomical relations in the wounded eye, that were described previously (displacement

of the interior membranes, wrong joining up, disturbance of the blood circulation). All this is due to the fact that the surgeon does not pay much attention to the state of the wound when operating by Kuhnt's method. And this is the basic defect of this operation. Parallel with the yawning of the wound one sees a bad adaptation of the edges of the wound even when they are near one another. We have to point out that these edges (scleral as well as corneal) are rarely traumatised even with large wounds, and if sometimes one sees their splitting infiltration, or necrosis, then even at a small distance from the edges of the wound the membranes themselves are in a good condition. But generally speaking the correct apposition of the edges of the wound is extremely rare. In the overwhelming majority they are superimposed one on the top of another, or are healing up at an angle or are inverted into the anterior chamber; sometimes only one edge, sometimes both, as the result of the pull by scar formation or by folding and so further inversion. But in small wounds, operated on by Kuhnt's method, the yawning of the wound was small, and one would think that the flap of the conjunctiva would fix them satisfactorily. And clinically the healing up in those cases was going on smoothly and finished with a scar that looked good on the surface, but in those eyes that were enucleated later on was noticed a peculiar irritation, hyperaemia of the iris, miosis (exudation was rare), ciliary pains and, what is very characteristic, still later a flattening or even a subsidence of the surface, where the scar is situated—usually labelled as atrophia bulbi incipiens and the above described symptoms as the early stage of sympathetic ophthalmia. And with the diagnosis of traumatic iridocyclitis these eyes are enucleated. On microscopical examination one sees the previously described phenomena produced by the conjunctiva, epithelium and edges of the wound—all of them—less traumatised than in other cases and insignificantly changed; as far as the adaptation is concerned—in small wounds with a displacement of the edges—their adaptation is rarely a correct one. Together with the described changes, we saw in similar cases some interesting phenomena usually seen with Kuhnt's operation. We see a superficial joining of the edges of the wound and a good healing up of the superficial layers of the cornea with a hardly noticeable scar, nearly by first intention. By clinical examination from the external surface the defect is completely covered by epithelium and the scar looks perfect. But the healing up involves only the superficial layers and through the substantia propria, as a rule, the edges of the wound are not joined. And so the edges of a small wound, joined at the surface, gradually separate deeper—the deeper, the more so—and so in the picture of regeneration one sees always the figure of a triangle, with a base

towards the anterior chamber. This characteristic triangle, better or worse according to the section, was seen by us in more than 90 per cent. of all examined cases of Kuhnt's operation in small perforating wounds.

What is the meaning of this geometrical design? Its sides, equal in size, are representing the edges of the cornea; they limit the triangular defect very quickly, and even in the first 4—5 days the defect is fully filled up by new-formed tissue, growing from the edges of the wound. In the superficial layers, where the yawning is small, this tissue is insignificant, but the deeper it becomes the larger, according to the separated edges of the wound, forming whole layers on the internal surface of the cornea. In cases where there are defects of the endothelium of the membrane described, and also on the surface of the iris, it encapsulates the anterior chamber, penetrates deeper in the posterior chamber and sometimes even deep into the cavity of the eye, on the way soldering to itself all objects that it meets—iris, ciliary body, remnants of the lens.

Later on these bands become shorter and produce detachments of other membranes and a flattening of the surface of the sclera.

The anterior part of the uvea usually remains passive in this independent and powerful process of the super-regeneration, and the iris and ciliary body are only taken in by this rapidly growing tissue, but the signs of inflammation or exudation are absent. That is why we cannot reckon the clinical signs to be an iridocyclitis, and we will in the future have to reserve our opinion in this respect, taking into consideration the described morphological changes, that produce a compression, folding up and irritation of the eye, due to these powerful pulls on the inside of the sclera, that are seen clinically on the surface of the globe.

Coming back to the analysis of the methods used for covering the wound I have to examine the cases where no surgical measures at all were applied and the wound was left untreated. The result was even more unfortunate than with Kuhnt's operation, where at least an attempt was made to join the edges of the wound by a conjunctival flap. The yawning of the wound is larger; the edges of the wound are folded; and all the described complications are much worse. This is why the wound ought to be stitched up even in cases of very severe trauma. From the point of view of the anatomical approach the failure to join together or fix by one or other method the edges of the wound—even in large ones—means negligence in taking all the necessary steps to save the eye. Do we succeed in all that when operating according to Kuhnt? Following the well-known technique of this operation with all its modifications we have to conclude that the efforts of the surgeon are directed against the infection, but not to the fortification of the edges of the wound.

It is evident that if the above described triangular defect in the wound could be abolished and properly sutured by strong sutures, the regeneration of the wound would proceed within normal limits. It always happens when the edges of the wound are correctly joined. But in the cases where the regeneration process became ultra-powerful, in spite of the absence of infection or of danger of sympathetic ophthalmia, in spite of the relative insignificance of the wound itself, the eye was lost only because in our surgical

FIG. 1

The wound after Kuhnt's operation. The edges of the wound are displaced, one of them is covered from the surface by the debris of the conjunctiva. Both edges are covered with epithelium, on one of them is proliferation of the epithelium along its surface, this edge is inverted.

FIG. 2.

After Kuhnt's operation. The edges of the sclera are wrongly joined, are superimposed and taken in by the scar tissue.

measures in such cases, particularly when Kuhnt's method was employed, we neglected the necessary approach and so allowed a very frequent complication to arise.

This is why especially under battle conditions we have to resist the temptation of applying Kuhnt's method and/or to cease to use it completely, or to use it only in exceptional cases. The popularity of this operation at present gives to the surgeon the sensation of

FIG. 3.

The triangle after Kuhnt's operation. The surface of the wound is closed, in the depth the edges of the wound gradually separate, forming a triangular defect that is filled up by scar tissue growing from the edges of the wound. The scar penetrates into the anterior chamber, forms a wide powerful band, growing deep into the cavity of the eye. *On one side, the iris is taken in* by the scar tissue.

FIG. 4.

A similar picture from another operation of Kuhnt.

safety and so limits his activity in the individualisation of his approach that was recommended by Kühnt himself. As a result of our analysis, the basic requirement of our surgical measures ought to be a solid joining of the edges of the wound on the surface and in the depth right through. And the most advisable would be scleral and corneal sutures always with a prior excision of the all prolapsed membranes. After removing all elements that may be in the way of the healing up of the wound we have

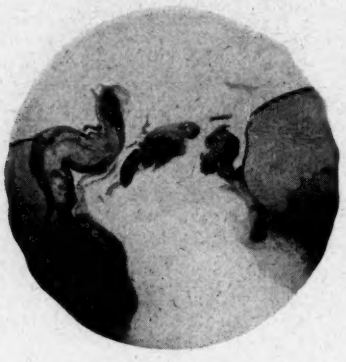

FIG. 5.

No surgical measures were taken. The edges of the wound are widely separated. The iris is prolapsed and is joined to one edge of the wound. The other edge is covered with epithelium.

to join the edges of the wound so as to have a complete adaptation and to try to fix them in this position by strong sutures.

Must these sutures be dia-scleral or deep scleral right through the whole thickness of the sclera, or cornea, more or less deep? This question must still be studied by experiments on animals because even the technique of such sutures is little known at present, judging by the literature of the subject.

Such is the present position of this method. These views are not only reckoned to be obligatory—I speak only about the large wounds—but judging by the literature are not widely applied in Russia or abroad. Müller, in his previously mentioned work, recommended the applying of sutures in 1945 and said that whoever will apply this method will be surprised by the number of favourable results in comparison with cases where the wound is left to the natural process of scar formation. The fact that till now we have still to persuade surgeons to use this method was the reason of the writer of this paper reading no fewer than ten papers at different scientific societies during the war years.

And during the war years the Russian surgeons became more critical about Kuhnt's operation (Prof. Strachoff was always against it) and some advocated application of sutures (Katznelson, Kopp, Longinoff, Chechik-Kunina, etc.). In the Institute of Helmholtz there is a great change of opinion in favour of stitching and frequently the results are brilliant. In Dr. Chechick-Kunina women's department all wounds of the cornea and sclera are always stitched up and comparing with last year, when the majority of the cases were operated by Kuhnt's method, the frequency of enucleations fell by 8·9 per cent.

The ophthalmic surgeons in the near future will undoubtedly work out a rational surgical method of healing up eye wounds helped by the pathologico-anatomist. The duty of the latter is to show the unsatisfactory state of the matter, to give it a new basis and the right direction.

PART II

THE important question—when discussing perforating wounds of the eye—is the process of regeneration of these wounds. As was indicated in my previous paper there are peculiarities in the process of the healing of wounds of the eye, that are of enormous theoretical and practical interest for an ophthalmic surgeon, but the importance of those details is usually not realised when treating a wounded eye. And because of that the process of regeneration, which is necessary and important in every wounded eye, becomes not a bene-, but a malevolent factor. When the sclera and especially the cornea are perforated, the regeneration of them goes on in its own peculiar way, dissimilar from the usual granulation of connective tissues. First of all the blood vessels do not take any part in it; they are of course absent in a normal cornea, and in cases of keratitis of different origins, including the traumatic ones, the vessels penetrate into the cornea from the peripheral net. But the walls of the vessels remain passive in the process of regeneration and the latter can go on with a complete absence of blood vessels. This is contrary to the usual process of the connective tissue, where the regeneration usually goes per fibro-vascular way. However, we do not see here the usual morphological picture of the usual cycle-development of granular tissue—the young immature cellular elements of the connective tissue with their later differentiation are absent. We saw, in fact, on wounds in man and in experiment on animals, where the wound, even 2 to 3 days after the trauma, is already filled up by narrow and long fibroblastic cells.

According to Wolfram and Boenig, Hañke and experiments of

Zazybiñ and Plitas, also of our own, it may be reckoned as proved, that the regeneration of the cornea is due to the proliferation of the corneal cells. The epithelium, to which the older authors starting from Donders ascribed the principal rôle, is of no importance in this process—it plays quite a different part. Nor is the episclera of much importance, or suprachoroidea or conjunctiva, contrary to opinions of other authors, including the writer herself—in her work on pathological anatomical changes after Gonin's operation (*Arch. f. Ophthal.*, 1935).

It is clear for us now that they take no active part in the cicatrisation and are not a plastic material for the regeneration of the sclera or cornea.

Our own researches in the regeneration of the cornea are partly connected with the morphology of the new tissue, but chiefly with the dynamics of the regeneration; we first saw it in the experiment with the transplantation of the cornea in the anterior chamber of rabbits (report read during the fourth session of the Central Ophthalmic Institute in Moscow).

I perforated the cornea of the rabbit and introduced at the same time in the anterior chamber pieces of the cornea of rather large dimensions; because the implanted piece was so large, I had to use some force to introduce it in the anterior chamber and so the edges of the wound were badly traumatised. As a result the implanted piece already on the fifth day—the earliest date of enucleation—was completely surrounded with new formed tissue, starting from the corneal scar, the scar itself by this time being already properly formed.

In this experiment we watched chiefly the implanted object; but the above described tissue was in the way and with the view of the isolation of the graft we started to introduce it through the pupil into the posterior chamber, but the quickly growing scar-tissue penetrated there too, surrounded it, and also any other organs in its way—iris and the lens, for instance—and penetrated deeply inside the eye, in a horizontal direction, up to the ora serrata, and further, and so we could not isolate ourselves from this tempestuous growing tissue. This first made me study this extraordinary energy of growth of the corneal scar and also some other peculiarities—and these were the basis of our further studies of the regeneration of the sclera and cornea in cases of trauma of the eye.

The above described experiment with the transplantation of the cornea entirely corresponds to the wounds of the eye, our graft being similar to the foreign body, together with a considerable traumatisation of the edges of the wound.

When analysing the further stages of the regeneration, by studying eyes enucleated because of wounds of the cornea, we see how

the scar tissue, growing towards the deep inside of the eye, penetrates everywhere, where it does not meet any obstacles—first of all into the anterior chamber, where the foreign body itself already prepared the way. Here this scar-tissue at once becomes much larger, first because it is joined by new tissue—if Descemet's membrane and endothelium are also wounded—and secondly, because its own cells proliferate so quickly; this later process can be especially clearly seen on the periphery where the scar-tissue is in contact with the aqueous. Becoming very powerful, sometimes having the form of a band, the new formed tissue penetrates the posterior chamber, first going round and later enclosing the lens, and goes still deeper; and if the lens is also wounded, it provides a further stimulus for this new formed tissue. In some cases, this tissue follows the route of the wound right through the eye up to its posterior part. It has such a characteristic form, because the cells are basophilic in the initial stage, and especially because of their fibre-like structure, that with some experience you can recognise it even with a weak magnification. It is entirely different from the products of organisation and inflammation of the wounded eye, which are joined frequently in some degree to this basic process.

Later on the number of the cells in this tissue diminishes, they are less basophile; the tissue looks more pink, like the mature corneal tissue, sometimes structured even in real layers like a normal cornea. This final metamorphosis is the witness of organogenesis—very interesting from a theoretical point of view.

At present we will discuss chiefly the phenomena of practical interest to an ophthalmic surgeon; such is the presence of the regenerative tissue in the anterior chamber and the resulting increase of the intra-ocular pressure in a wounded eye. It is necessary to add that this produces one of the worst forms of secondary glaucoma. It is caused by the fact that the scar-tissue, after penetrating the anterior chamber produces whole layers of new tissue not only on the posterior surface of the cornea, but also on the anterior surface of the iris and so closes the angle of the anterior chamber and encapsulates the whole chamber altogether. Compared with other factors that usually close the angle of the anterior chamber, like the ordinary synechia, hyphaema, exudation—even the changes in the configuration of the iris, where it is possible for some holes still to be left free—the above described process is extremely dangerous, because with the encapsulation of the anterior chamber by this scar-tissue the angle is closed completely and it is obvious that in those cases all our therapeutic measures are useless, because this kind of tissue is not capable of being absorbed—like some of the other indicated pathological phenomena.

It is worth while mentioning here that a similar encapsulation

of the anterior chamber occurs by the ingrowing into it of the epithelium penetrating by proliferation from the wound. In those cases the anterior chamber is covered by a delicate veil of one layer of epithelium that can be seen only under a microscope. You cannot see it through the slit-lamp, while the more solid regeneration-tissue in band-form connected with the scar can be seen easily sometimes even with ordinary focal illumination, and it is this tissue that is sometimes erroneously diagnosed clinically, as exudation, pus, secluding tissue, etc.

I will speak only shortly about regeneration of the wounds of the sclera, because the principal processes are the same as in the cornea. The same stormy hyperproduction of regeneration tissue can be seen. It shows itself in the tendency of the scar to go deep into the eye by powerful bands or layers, going very far away from the perforating wound of the sclera. En route, this tissue, as in the anterior part of the eye, goes round all objects that it meets, and the latter also take some part in the process. You can make very interesting observations on different membranes of the eye—their morphological and potential peculiarities; their interaction with the basic process. But it is only a detail in the overwhelming process of fibromatosis. The bands, arising straight from the scar, could be so big as to go right across the eye, sometimes filling up completely the interior space, deforming, separating and growing into other membranes. The infiltration at this stage may be quite insignificant, if the eye is not infected and if the process does not go on towards sympathetic inflammation.

We have to point out that we see a similar process on the sclera after diascleral removal of foreign bodies, when the whole success of this operation is annulled by the described complications. The degree of the trauma to the sclera is the deciding factor. We do not think that the epithelium plays such an important part as was ascribed to it years ago.

But still there is a difference in the regeneration of the sclera and of the cornea. In the former we do not see what I have described, the struggle with the gradual alienation of the deeper layers, that is often seen in the cornea, especially after Kuhnt's operation. The wound of the sclera forms a defect of equal dimensions right through the membrane—a difference that undoubtedly depends on the anatomical peculiarities of those two membranes, especially the presence of Descemet's membrane, whose elasticity produces the gradual compression of the deeper layer—a process not seen in the sclera, where a similar membrane does not exist. In all surgical measures this difference must be remembered and this is why deep corneal sutures are even more necessary than deep scleral.

The
C. DAVIS
Keeler
SPRING FITTING

REVERSIBLE
OCCLUDER

Ideally suitable for use in a consulting room for Perimetry and Scotometry when interchange of occlusion is required. The spring fitting allows for this interchange without greatly disturbing the patient's hair.

C. DAVIS
Keeler LTD
OCULISTS : DISPENSERS
47 WIGMORE ST. LONDON W.1.
BRANCHES AT
BIRMINGHAM : PLYMOUTH : TRURO : BRIGHTON : BURTON ON TRENT
WEST BROMWICH : FALMOUTH : PENZANCE : ST. AUSTELL : REDRUTH

MELSON WINGATE LTD.

Dispensing Opticians,

7, WIGMORE STREET,
LONDON, W.1.

and of

5, Broad Street, Oxford,
35, Brook Street, Bath,
29, Mount Pleasant, Tunbridge Wells,
52, London Road, Sevenoaks,
28, Poole Hill, Bournemouth,
707, Christchurch Road, Boscombe,
109, St. Mary's Street, Weymouth,
40, Gt. Western Road, Dorchester,
138, High Street, Poole,
10a, Union Street, Yeovil,
68, Monarch Parade, Mitcham.

The services of Qualified and Experienced Optical Dispensers are always at the disposal of Ophthalmic Surgeons and their patients at the above addresses.

What do we see clinically in the typical cases of this regeneration? Frequently these are small perforating wounds, limited to the anterior part of the eye, with a well healed-up small external scar, with a stubborn continuous irritation that instils in the mind of the surgeon the fear of sympathetic ophthalmia and usually such eyes are enucleated with the diagnosis of traumatic iridocyclitis.

But the microscopical examination in this kind of trauma usually does not confirm these fears in the majority of cases: the inflammatory-exudative, and especially infiltrative processes in the iris and ciliary body are usually insignificant; the sympathetic process is seen only in 2-3 per cent.; intermediate forms are normal (10 to 12 per cent.); the primary importance belongs to the described super-regeneration process, whose particulars are so similar that they are becoming an artefact, being different only in some details, but not in essence. The iris and ciliary body usually remain passive; the reaction in them is insignificant; the iris and ciliary body are only joined to the super-regeneration tissue round them with consequent atrophy of their elements, and the clinical diagnosis of traumatic iridocyclitis in those cases proves to be a wrong one. And this general all-embracing clinical diagnosis is not exhausted by the pathological process of the anterior part of the eye. *And so, in cases of the above described changes in the wounded eye, we see an absolutely separate independent process, not noticed yet up till today, but with a peculiar tendency of its own.*

Proliferation of powerful bands of tissue inside the eye leads to atrophy of the bulb. These bands are the immediate continuation of the scar and are the products of super-regeneration of the wound.

How often do we see this process destroy the eye without evidence of other pathological changes? According to the statistics of our pathological histological department of war wounds, and also that of civilian wounds for 1943 (415 enucleated eyes) the above described traumatic process was seen in 23 per cent. (in civilian category in 29 per cent.). For battle wounds where the trauma is more heavy, where an increasing percentage perishes from the traumatic moment itself, the percentage is a little lower—16 per cent.

This shows that we are describing a factor of major importance, especially if we consider the higher percentage of blindness in perforating wounds of the eye, shown by the latest statistics (Preobrajenskaja, G.N.).

The grave danger to the eye from perforating wounds makes us pay special attention to the causes of this danger and to the measures to fight them.

This super-regeneration process, the principal one in more than 20 per cent. of enucleations, is an important object of study that will attract our attention in the near future.

Can we indicate now any points for the clinician? How to differentiate between this process and the other one, with the real danger of sympathetic ophthalmia? We think that we can indicate already one symptom, when with a long-standing irritation, we see on the surface of the bulb flattening, falling-in, sometimes even a pull from inside of this or any other part of the sclera or cornea, that coincides with the localisation of the scar. In those cases the sclera loses its peculiar globe-like form, sometimes in limited spots, sometimes on the large surface of the sclera; especially characteristic is this picture on the limbus, where the peripheral part of the cornea seems to be cut off, being drawn inside.

These phenomena, verified microscopically, show without any doubt that in this particular globe are present powerful agents, capable of deforming the bulb in the locality of the scar, consequently the process is due to super-regeneration and—as a result of a dense fibrosis with a consequent scar formation—deformation of the surface of the eye takes place. In this case the whole symptom complex, suspicious as to sympathetic ophthalmia, may be referred to the above described fibromatosis, that has nothing in common with the sympathetic one, and where the irritation and painfulness are probably due to compression and scar formation and therefore natural irritation of the nervous apparatus of the eye; this is, of course, merely a proposition, and we will have to verify it on the morphological and physiological analysis of the nervous tissue of such eyes. But clinically there is a good deal of similarity between these two processes, which are really quite different in their substance and we hope that in the crystallisation of the diagnosis the clinician will add many new points.

We must understand the peculiarities of this process, its morphology and pathogenesis to be able to fight successfully. Special attention ought to be paid to the structure of the scar; its extraordinarily quick and powerful growth, especially after the anterior chamber is penetrated, where there is a liquid milieu; also when the edges of the wound are separated or form an entropion, *i.e.*, their wound surface is facing the anterior chamber. In those circumstances this process becomes very intensive. The same intensification is seen when this regenerating tissue comes in contact with the substance of the lens, when its capsule is wounded—I described that previously; it seems to give an extra stimulus to the growing tissue.

All these circumstances are bringing us to the conclusion that *the regeneration of both sclera and cornea are proliferative processes*, where similar conditions are necessary—a liquid milieu, a *good nutritive substitute, are for the cultures of tissues in vivo*, but of the types of such cultures *in vitro*.

Our researches on the changes in the eye lead to the consideration of the eye as of a highly organised camera, where may be developed similar reactions. (This was recognised a long time ago, under the name of " autonomy of the eye "—translator's remark). The presence of good nutritive media, helped by the fibrin of the haemorrhage and its solution, products of eye-tissues damaged by the trauma, and, besides, the constant temperature and closed cavities—all these are conditions favourable for creating an " exclusive " chamber, but in addition with constant metabolism; in this connection we see in the eye the inflammatory processes and at the same time the purely proliferative ones, peculiar to the eye, as to a closed cavity containing liquid milieux of different chemical composition.

For a long time now histology has been busy with the growth and preservation of neoplasms and other tissue-elements—in the anterior chamber and the eye of animals. Unfortunately ophthalmology up till now did not appreciate the meaning of those experiments for better understanding of the pathological processes in the wounded eye, rather peculiar to this organ, as discussed above.

In 1941 in my paper on " spontaneous cultures of the tissue inside the eye" (Vestn. Ophthalm. Vol. XVIII, A. 5), I pointed out that—parallel to inflammatory processes and their reactions—in the eye take place also proliferative processes, peculiar to the eye, as a viscus where are present liquid milieus; a similar phenomenon was described by me in the enucleated eyes in different diseases, but seen quite by chance. We see most frequently in trauma of the eye (but also in other diseases), that the tissue elements show a real cytotypic growth, so characteristic in the tissue cultures *in vitro*. For instance, I described the presence in the anterior chamber of a culture of Schwann's cells, developed from the iris, probably from the sphincter, where are present ectodermal elements; this culture covered like a delicate veil the whole anterior chamber. Cultures of pigment-epithelium are seen frequently, proceding into the cavity of the eye from the retinal pigment, or into the anterior chamber from the pigment epithelium of the iris; cultures of ciliary epithelium, lenticular capsule, etc. In the cavity of the eye the elements of the detached retina frequently show signs of intensive proliferation, and in accordance with the nature of this process and consequent variation of the exudation, the proliferation affects different elements of the retina. We saw also a typical growth of fibroblasts from a scleral scar in cases of war wounds. And, lastly, displaced pieces of the membranes of the eye act as a real source of tissue cultures; far removed sometimes from their primary location and meeting favourable conditions in the liquid

milieu they produce epithelium and continue to exist for many years.

I discussed all these questions because I wanted to make clear the development of this stormy regeneration process in the eye, impossible to understand otherwise. The uniform structure, extraordinary quickness of growth, conditions favourable to direct this growth deep inside the eye—those are reasons to reckon it as a culture of tissue, although some characteristics of the cytotypic growth are absent. But on the periphery of the quickly growing, very tight, brush-like band of the fibrous type tissue, in the places where it grows more free and comes in contact with a liquid milieu, one can see a different structure and separate figures of typical star-like fibroblasts, very similar to those we see in the scleral scar. Narrow, thin, arrow-like cellular elements, separating themselves from the common band and entering the liquid milieu look like typical elements of a growing tissue-culture.

When staining these spots for the intercellular tissue by the method of Snesarev it is seen that we have to deal with fine argentophyl fibrils, with the collagenous ones beginning to appear, and their disposition has an irregular mixed up character—and all of these not characteristic of a fibro-vascular type of regenerative connective tissue, but peculiar to the conduct of the inter-cellular substance in the tissue-cultures. This was also the opinion of Prof. Snesarev, in whose laboratory my preparations were stained, and for whose help I am profoundly thankful.

What are the practical deductions of this reorientation of the surplus growing regenerative tissues of the external membranes of the eye towards tissue-cultures? We have to use the experience of the scientists, who are working with the method of tissue-cultures, because they have worked out a whole host of conditions, favourable to the growth of tissue elements and *vice versa*. From our point of view we are advising not to allow the presence in the wound of the liquid milieu, of the nutritious medium, like lenticular masses—and especially we have to fight—when healing up the wound—against the penetration of the regenerative tissue into the anterior chamber, *i.e.*, a proper closing of the wound is the first condition of a good result. Besides that we have to try to regulate and to depress the regenerative process by chemical and other methods, not only different from those that are usually employed for the stimulation of wounds, but taking into consideration the peculiarities of the above described process.

In the first paper we have made already corresponding practical suggestions about the necessity of active surgical methods when treating a wounded eye: as soon as possible we have to reconstruct the damaged co-ordination and to sew together the

edges of the wound. The analysis of the regeneration-process points to the importance of detailisation of this method, because it is not sufficient to put stitches on the sclera or cornea—it ought to be done in such a way that the edges of the wound are close together, with the correct adaptation, and right through the whole depth of the wound.

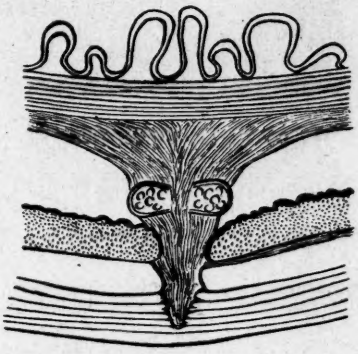

FIG. 6.

A scheme of corneal regeneration—starting from the triangular scar, the band grows gradually thicker and penetrates deep into the vitreous. On its way it takes in the iris, goes right through the traumatised lens and forms a powerful layer structurally similar to the corneal substance. It joins and detaches the retina.

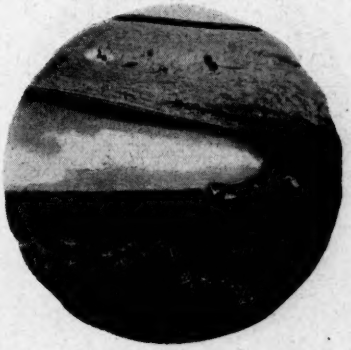

FIG 7.

Encapsulation of the anterior chamber by a band of new formed tissue (on the right), that goes round the angle of the chamber and forms layers on the anterior surface of the iris.

FIG. 8.

A contracted scar of the cornea after Kuhnt's operation with proliferation of the epithelium from the surface. The edges of the wound are wrongly adapted; the left one is joined to the right one only in the upper part; further down the edges are separated, forming a triangle. A large band of newly formed tissue—a continuation of the scar grows into the interior. The more recent immature part of it can be seen with strong magnification in the following photo.

FIG. 9.

The inter-cellular substance of Fig. 8 stained by Snezarev's method. A mixed net of fine argentophyl fibrillae; here and there are passing single thicker collagen fibres.

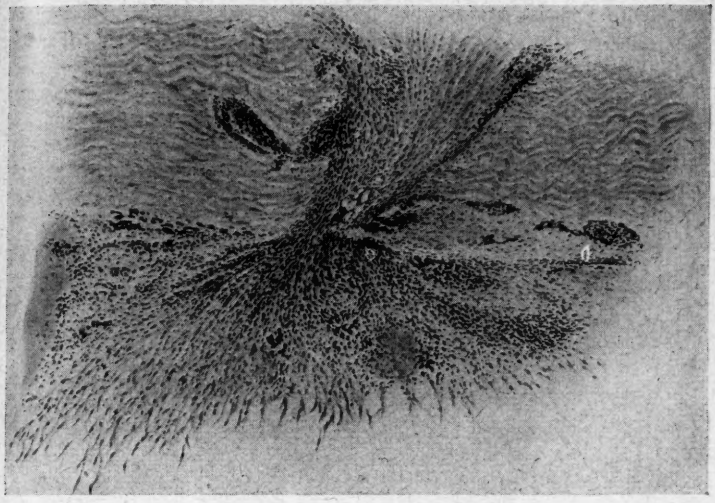

FIG. 10.

Scleral scar in a war wound. In its deep parts, in the liquid milieu of the perichoroidal space (the retina and choroid are detached)—a typical culture of fibroblasts.

FIG. 11.

The same cells with greater magnification.

Unfortunately I cannot mention in the present paper a host of clinical instances and illustrations—they would form a whole atlas—where an incomplete closure of the wound and irregular adaptation of the edges with their entropion in the anterior chamber, and especially their transmutisation, are the source of powerful layers and bands inside the cavity of the eye.

But, even with all that in mind, we have to study a whole range of separate moments in the healing of the wound before we shall be able finally to adopt a method of stitching.

FIG. 12.

In the wounded eye, from the scar of the iris, a fine veil of tissue attached to the interior (posterior) surface of the cornea, grows into the anterior chamber.

FIG. 13.

The same veil with greater magnification.

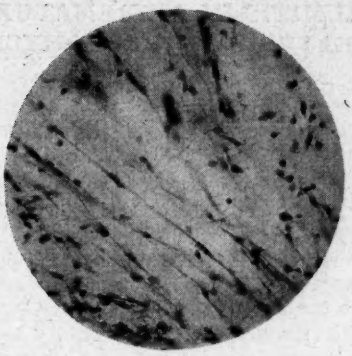

FIG. 14.

Cellular elements of the same cultures.

These are my conclusions :—

(1) The regeneration of the sclera and cornea is not the ordinary granulation process of connective tissue, that is going by the fibro-vascular way, with its peculiar cycle of development of the cellular elements, but a proliferation *sui generis* of similar cellular forms that morphologically are near to tissue cultures.

(2) The dynamics of this process are characterised by an extra-ordinary intensity, as a result of which—in unfavourable conditions—is seen a surplus-growth, chiefly as a result of the penetration of the regenerative tissue in the liquid milieux of the eye.

(3) Following the described peculiarities of this process and the idea that the eye, as a closed chamber, is ideally adapted for tissue-cultures *in vitro*—we ought to use the experience of histologists and their ability to regulate the growth of the tissue-elements.

(4) We ought to undertake the clinical and experimental research of the best methods of closure of eye-wounds, and also of the regulation of the regenerative process of the healing of the wound; besides surgical perfection, we ought to treat it as analogous to the tissue-cultures.

(5) In connection with surplus regeneration of the eye-wound is seen an autonomous fibromatosis in the eye, pathologically quite a different form of disease, that has nothing in common with sympathetic ophthalmia, but clinically very similar to it, and with our present knowledge, still labelled under the common diagnosis of traumatic iridocyclitis, which ought to be differentiated from it in the future.

PANOPHTHALMITIS IN A PREMATURE INFANT TREATED BY STREPTOMYCIN*

BY

L. B. SOMERVILLE-LARGE

DUBLIN

THE FOLLOWING is an account of panophthalmitis in a premature infant caused by bacillus proteus and treated with streptomycin.

The patient was a male premature child weighing 4 lbs. 5 ozs. at birth. He was born in the Rotunda Hospital, and I was called to see him there in the Premature Ward when he was eleven days old. The ocular history was that inflammatory swelling in the lids of his left eye had commenced twenty-four hours previously and was rapidly increasing. He had had a superficial skin infection of his lower abdomen not reaching the umbilicus. This had cleared up rapidly on 30,000 units of penicillin injected over a twenty-four hour period, and was at that time completely cured. The umbilical cord had not fallen off. This separation occurs normally on the fifth or sixth day, but in this case was not complete until the twelfth. The baby was progressing satisfactorily, taking feeds well and putting on weight.

On examination of the condition I found an inflammatory oedema involving the lids of the left eye. This was well marked on the upper lid, but was only slightly apparent on the lower. The pre-auricular gland was not enlarged. The eye was proptosed. No conjunctival discharge was present. There was intense ciliary injection. The cornea was hazy. The anterior chamber was half full of hypopyon which lay over the pupil, no pupillary margin being visible. There was no red reflex. The condition was diagnosed as panophthalmitis with a possible infection of the orbit. Panophthalmitis occurring after birth is usually regarded as due to an infection of the umbilical cord. Its occurrence at this period of life is rare. No case has occurred in the Rotunda Hospital during the last twelve years (approximately 55,000 births). The right eye was normal.

Mr. R. R. Woods, the Ear, Nose and Throat Specialist to the hospital, kindly examined the case, but no source of possible nasal infection was found.

General examination revealed that the umbilicus was infected and also that there were two subcutaneous " abscesses " in the skin of the lower abdomen. These latter did not wholly resemble abscesses as they were not accompanied by signs of inflammation

* Received for publication, March 29, 1947.

but appeared rather as small herniations through the abdominal wall. They were, however, aspirated for examination. A swab was taken from the umbilicus. Both examinations revealed bacillus proteus in pure culture. It was considered that the primary infection had taken place through the umbilicus.

Immediate operative treatment consisted in passing a fine Graefe knife into the orbit, and a search being made with a probe for pus. No pus was found. The proptosis remained unchanged. Three days later a needle was inserted into the anterior chamber and pus removed for bacterial examination. Here again bacillus proteus was grown in pure culture.

Immediate therapeutic treatment consisted in the administration of sulphadiazine by mouth and penicillin by injection. A total of fifteen grammes of the former and 170,000 units of the latter were given within the first six days, when they were discontinued and streptomycin started. The bacillus proteus proved bacteriologically to be resistant to penicillin.

During the first six days under the above therapy the ocular condition became steadily worse. Severe oedema developed in both

FIG. 1.

FIG. 2.

lids. The conjunctival vessels became very congested and pannus commenced above. This pannus eventually covered the upper third of the cornea, and superficial blood vessels also encroached on the rest of the corneal periphery. The centre of the cornea developed a deep opacity. The child's general condition, however, remained highly satisfactory. There was no rise of temperature and weight was gained steadily.

Bacillus proteus is resistant to penicillin and the sulpha drugs but is highly sensitive to streptomycin. There was some delay in getting this drug, and no information as to dosage in a premature child could be obtained. Treatment was carried out as follows: One gramme of streptomycin was dissolved in 10 c.c. of sterile water and 1 c.c. was injected intramuscularly every three hours. This was continued for twenty-one hours, when the dose was reduced to 0·5 c.c., which was given three-hourly for sixty-six hours. Towards the end of this period the baby was bottle feeding so slowly that tube feeding had to be started. There was also a loss of weight (from 4 lbs. 14 ozs. to 4 lbs. 12 ozs.) and a rise in temperature (99·8 to 100°) for two days. It was uncertain whether

these symptoms were due to streptomycin, but some reduction was thought advisable. The dosage was therefore reduced to 0·25 c.c. every three hours, and this was continued until a total dosage of two and a half grammes had been given. The treatment with streptomycin covered a period of six and a half days.

Streptomycin was commenced at 3 p.m. one afternoon, and on the following morning for the first time there was a marked improvement in the clinical appearance. The lid oedema had greatly subsided and the eye was open. On the second day the skin folds had returned, and on the third all inflammation had gone from the lids leaving only some slight oedema. The condition of the eye itself remained unchanged. The subcutaneous abscesses disappeared soon after the streptomycin was commenced and required no local treatment.

On the ninth day from the commencement of streptomycin the globe perforated at about six mm. from the limbus between the inferior and lateral recti. Evisceration was carried out on the same day. The vitreous was found to be grossly infected. Swabs from the site of perforation, from the anterior chamber, and from the vitreous were taken. All were found to be sterile on culture.

The pathological report on the cornea and uveal tissue removed is as follows:—

The piece of cornea sectioned shows a considerable amount of proliferation of the epithelium. At one point this epithelium and Bowman's membrane have been broken through by a haemorrhage coming from a new vessel lying just under Bowman's membrane. A considerable number of new vessels can be seen at different levels, the majority lying anteriorly. Scattered chronic inflammatory cells are present mostly in the anterior third. At one point there is an aggregation of these cells involving the neighbourhood of Descemet's membrane and the posterior fourth of the adjacent substantia propria. In another area the whole corneal thickness is diffusely infiltrated with chronic inflammatory cells. The piece of uveal tissue consists mainly of choroid—a small part of the ciliary body is also present. The entire tissue is infiltrated uniformly, but not heavily, with chronic inflammatory cells, round, plasma and epithelioid. Some polymorphs are also present suggesting that the active inflammatory phase had not completely passed. Normal choroidal structure is unrecognisable. Proliferated pigment is present, passing through the section. Blood vessels are very numerous, the greater number containing erythrocytes. Some scattered haemorrhages are also present.

By the finding of bacillus proteus in the anterior chamber (in pure culture) prior to commencement of streptomycin treatment, and by the negative cultures obtained from the highly infected

globe after treatment, it may be inferred that this drug is capable of permeating the uveal tissue.

It is of importance that infection of the umbilical cord by a non-virulent organism is capable of producing panophthalmitis, and this without any general symptoms of septicaemia. Meningitis can, however, occur in infants from bacillus proteus, and this was a complication that was feared in this case.

The child is now three and a half months old, has remained in perfect health and is gaining weight steadily. No ill effects from the streptomycin treatment are apparent.

Summary

A case of panophthalmitis in a premature child following umbilical cord infection by bacillus proteus is described. An account is given of the treatment with streptomycin which is considered to have overcome the inflammation in the uveal tissue.

I am grateful to Dr. Ninian Falkiner, Master of The Rotunda, and Dr. R. Collis, Paedriatician to the hospital, for their advice and permission to publish this case. To Dr. Hinkston's invaluable assistance, and to Sister Moran who looked after the case I am greatly indebted. I am much obliged to Miss Thompson for her fine photographs, and to Dr. McCrea who kindly carried out the pathological examination.

ON MENINGEAL REACTIONS IN SYMPATHETIC OPHTHALMITIS*

BY

L. CORCELLE

AGEN, FRANCE

IN 1934† I showed for the first time that meningeal reactions occurred in the course of sympathetic ophthalmitis, of which the interest is such as to warrant fresh emphasis. Before my paper appeared we had recognised the extra-ocular complications of sympathetic ophthalmitis, but their frequency was not very great and their description so very changeable that they were considered to be of secondary importance by most authors. However, Coppez, in his article on sympathetic ophthalmitis in the last *Traite d'ophtalmologie français*, gave them a few lines and cast doubts on

* Received for publication, January, 1947.

† Contribution à l'etude de l'ophtalmie sympathique. L. Corcelle, Thése, Bordeaux, 1939.

their nature. However, deafness, studied by Garrigou, Snellen, Rogman, de Wecker, Peters, Patry, Blatschech, Komoto, Truc, Serege, Sgrosso, and Calogero, was well understood. The importance of this complication, it is true, is variable and has escaped those authors who only studied the pathology of the disease. It should be remembered because one must suppose that the cause—allergy or infection—is susceptible of overrunning the framework of ocular pathology. On the other hand several very troublesome neurological complications have been observed.

Risley, Galezowski, Deutschmann and Mooren have reported the occurrence of convulsions. Delirium has been noted (Deutschmann, Terson, Sérège).

Colin and Duthil have published a case of severe sympathetic ophthalmitis with a spinal syndrome, pains and fibrillary contractions. The word meningitis has rarely been used. Renard, alone, has suggested it.

Snellen and Sérège have published observations where they use the term meningitis, but they did not examine the cerebro-spinal fluid of their patients.

Also my own observations were the first to allow of the affirmation of a meningeal reaction in sympathetic ophthalmitis. They appear to have received confirmation since their publication and it is actually possible to draw up a balance sheet of the new knowledge they represent and the importance of which can no longer be neglected.

Here is an account of three particularly typical cases to establish the good foundation of their existence.

Case 1. A Spanish workman, aged 63 years, sustained an accident at his work on January 28, 1933. A block of wood struck him in the region of the right orbit. He immediately complained of great pain and that he could not see with the damaged eye.

Examination showed: R.E. large hyphaema, dilated immobile pupil, lens luxated into the anterior chamber, no wound of the eye. T. −1·0. V. = P.L. L. eye, normal.

General examination disclosed renal insufficiency. Blood examination, normal. Negative serological tests for syphilis.

February 1, 1933. The lens was extracted by Snellen's scoop: slight loss of vitreous. The after-course was not satisfactory. The operation wound did not heal well; a prolapse of iris persisted in the upper part of the wound, pericorneal injection was very intense.

February 2. Hypopyon. The blind inflamed eye was enucleated on March 4, 1933, that is 33 days after the accident and 31 after the lens extraction.

Three days later the patient complained of diminution of sight in the left eye. Vision was now 1/20. Grey exudate showed in the pupil and seclusion was practically total. Tension was normal.

At the same time the patient complained of a feeling of lassitude and some shivering fits. He had no rise of temperature. The sympathetic iritis progressed in spite of all treatment.

March 22. An iridectomy was performed but the gap was soon closed by exudation. The tension was subnormal. The patient became deaf and complained of headache. Neurological examination was entirely negative and in particular he showed no sign of meningitis. Lumbar puncture was performed on April 1, *i.e.*, 24 hours after the onset of sympathetic uveitis, and gave the following results.

Cytology, 17,512 (lymphocytes).

Benzoin colloidal, normal. Albumen, 0·30: glucose, 0·75: chlorides, 7·40.

Twelve days later a fresh examination showed:

Cytology, 4,654 elements. Albumen, 0·30: glucose, 0·78: chlorides, 7·30.

On April 28, the vision was totally abolished, the eye was atrophied and the patient attempted to commit suicide.

Microscopical examination of the enucleated eye showed nodular leucocytic infiltration in the operation wound forming the "inoculation chancre" described by Redslob.

Case II. A man, aged 28 years, was wounded in the left eye on November 4, 1938, by a splinter of metal which perforated the front part of the eye.

On examination, there was a perforating scleral wound at "3 o'clock." In the wound was a small uveal prolapse and a bead of vitreous. Large hyphaema present. L.V.=0. Right eye, normal, V. 10/10.

On admission the uveal prolapse was cut off and the wound covered with a conjunctival flap. The after-course was normal, yet the eye remained blind. On January 4, 1939, it was decided to remove it, as signs of sympathetic irritation were apparent.

On January 15 the patient complained of limitation of sight in the right eye. Vision was found to be 8/10. Very intense pericorneal injection was present with precipitation on the posterior corneal surface, with posterior synechiae.

January 30. All signs increased in intensity. Vision, 1/10. Neurological examination negative. Lumbar puncture gave the following results:

Cytology, 63,3 lymphocytes: albumen, 0·50: glucose, 0·63: chlorides, 7·50.

Visual acuity improved to 10/10 on April 11. The patient considered himself cured and went back to work.

September 7, 1934. He presented signs of ocular hypertonus. T. +50. This yielded to medical treatment. Lumbar puncture gave normal figures.

Microscopical examination of the enucleated eye showed the anatomical lesions of "chancre of inoculation."

Case III. A man of 67 years of age, a healthy looking farm labourer was examined for the first time on June 27, 1946. He said that at the age of ten years he had sustained a perforating wound of the left eye. No surgical treatment had been undertaken and the globe retained merely poor perception of light. Four months before his visit to me he had received a fresh contusion of the left eye, but no perforation. Yet the globe became inflamed and painful and irido-cyclitis lasted a month. When "cured" perception of light was entirely absent.

After 3 months visual troubles began to affect the fellow eye. There was slight photophobia with vision reduced to 1/20.

Examination showed: Left eye, divergent, shrunken stump. The cornea showed deep greyish infiltration, with a number of new vessels.

The pupil was closed with old yellow exudate. There was complete seclusion with iris atrophy.

Right eye. Pericorneal inflammation. Many small precipitates on Descemet's membrane seen with the aid of the slit-lamp. Grey exudate rimmed the pupil and tied it down to the anterior lens capsule. The fundus was normal.

General examination showed nothing in particular. The examination of the nervous system was wholly negative. Lumbar puncture performed June 29, 1946, *i.e.*, 7 days after the onset of illness of the right eye, gave the following results:

"Cellule de Nageotte" 16, el 6 mm. 3, lymphocytes. Albumen, 0·60: glucose, 1·60: chlorides, 7·02. Khan and Meinicke reactions, negative.

June 29, 1946. Left eye enucleated. During the illness there was no fever.

July 7, 1946. Eight days after enucleation a second lumbar puncture was done with the following results:

"Cellule de Nageotte" 190, el mm. 3 (lymphocytes). Albumen, 0·80: glucose, 0·90: chlorides, 7·02. Blood sedimentation, 1st hour, 21 mm. Second hour, 43 mm. "Les Vernes resorcine: 17."

Between June 6 and August 8, 1946, the patient received 20 intravenous injections of sodium salicylate, of bevitine and 10 injections of staprolysat. The visual acuity was unaltered at the end of the treatment.

A third lumbar puncture was made on the 30th day of the disease and showed Cellule de Nageotte 32, el mm. 3. Albumen, 0·45: glucose, 0·45: chlorides 7·15.

At the present time the pupillary exudates are absorbed. The patient declares himself satisfied that the sight may be a little improved.

In the last three months I have seen two other cases of sympathetic ophthalmitis, the notes of which are as yet incomplete but they present meningeal reactions of the same kind. These observations have been confirmed by several authors.

In 1936 Espildora Luque found in 5 cases of sympathetic ophthalmitis a meningeal reaction traceable only through lumbar puncture.

In the first case there were 120 cells, in the second, 92, in the third, 5, in the fourth, 4, and in the last 20, but this author has not stated at what particular time the lumbar punctures were performed.

In 1945 Beauvieux and Bessiére published a note of a marked meningeal reaction with 543 lymphocytes.

In 1946 Touland reported to the Academy of Medicine four cases with meningeal reactions.

Legroux published a case with meningeal reaction of 8·8 lymphocytes on the 96th day of the disease.

Clinical Description

It is now possible to sketch the clinical picture of meningeal reactions in sympathetic ophthalmitis.

At the start there are no neurological signs. Headaches of frontal type have been stressed in some cases. (Beauvieux and Bessiére, Corcelle).

Espildora Luque has described them and mentions the possibility of vomiting, He thinks that headaches are the rule in the lymphocytic meningitis of sympathetic ophthalmitis.

Redslob has emphasised their importance. but has not established a relation with the meningeal reaction. When they exist they are of frontal type and very severe.

In Beauvieux and Bessiére's case they were occipital with exacerbation at night. They sometimes precede the onset of inflammation in the sympathising eye.

Deafness is frequently noticed. It does not appear always to be linked to the existence of a meningeal reaction. In six cases I have observed it thrice.

Vestibulary depression, which I have previously noticed, is to be found by systematic examination but it is inconstant.

One has also to mention the existence of a rise of temperature (38°C.) of short duration. The first and third of my cases showed a brief rise of temperature with general lassitude. These symptoms are inconstant and are not sufficient to warrant the existence of a meningeal reaction. Therefore the onset of lymphocytic meningitis is indicated by lumbar puncture. This has been done in fixing the

date of the appearance of clinical signs in the sympathising eye at the end of 24 days (Corcelle, 1); 15 days (Corcelle, 2); 7 days (Corcelle, 3); 10 days (Beauvieux and Bessiére); 96 days (Legroux).

One can affirm after these first results that the meningeal reaction may perhaps be regarded as contemporaneous with the appearance of clinical signs in the sympathising eye. In my 3rd case it was 166 elements on the 7th day, but by the 15th it had risen to 190 elements. By the 30th day it was 32 elements at which time the clinical signs were greatly improved. This evolution is not always calculated on that of the anatomico-ocular lesions. In Beauvieux and Bessiére's case it was massive (543 elements) but yet remained at 400 elements on the 74th day of the disease, when the affection seemed healed. The total number of lymphocytes in the C.S.F. appears proportional to the intensity of the affection. Grave cases are accompanied by a marked reaction but one cannot base a prognosis on it. However, in my first case I noted 174 elements and the patient became blind. In case 3 the meningeal reaction was 190 and the patient was cured. I have since seen a case in which the meningeal reaction was 88 elements which ended in blindness. Also in the case of Espildora Luque the numbers reached were few (56 or 21 elements) but we do not know enough of the clinical course in this case. Enucleation does not by any means influence the lymphocytic meningitis. In three of my published cases excision of the exciting eye was done when lumbar puncture allowed the study of the C.S.F. Conversely, excision could not be incriminated. In my third case the existence of lymphocytic meningitis had been proved before surgical intervention. Examination of the centrifugalised deposit is not the only interesting subject for study. Chemical examination offers particulars which I wish to emphasize. The albumen is usually normal, it can, however, rise proportionally to the numbers of lymphocytes: 0·80 for 190 elements and later 0·60 166 elements. On the other hand hyperglycosis in the C.S.F. is clearer. It was raised in my 3rd case to 1 gr. 80. In the other cases it remained at a lower figure.

Serological reactions for syphilis were negative in my cases. Espildora Luque in his cases noted 3 positive reactions.

Two points are of importance to be clear about in ending this description of the meningeal reactions in sympathetic ophthalmitis. Are these reactions constant and are they specific for sympathetic ophthalmitis?

The small number of published observations comprising an examination of the C.S.F. does not allow me to answer the first question in the affirmative. I know of a case where normal C.S.F. is mentioned, but the account does not permit any indication of the day of the disease when the lumbar puncture was made. In all

the cases I have seen in ten years I have always found a meningeal reaction.

Espildora Luque has examined the C.S.F. of patients suffering from a penetrating wound of the eye without finding very important modifications of the fluid, except in one case where a reaction of 3 elements existed and also a case of iridocyclitis of the damaged eye.

What is the meaning of this meningeal lymphocytosis ? One very interesting observation is that of Beauvieux and Bessiére for it comprises the existence of a retinal detachment, thus approximating sympathetic ophthalmitis to the syndrome of Karada. Now we know that this latter syndrome is itself accompanied by meningeal reactions, so it is logical to make this approximation, already presented by other authors (Magitot).

In a recent report devoted to uveitis of unknown origin* we have proposed considering sympathetic ophthalmitis as a lymphocytic uveo-meningitis.

This would appear to be due to a filtering virus as yet of unknown origin. The pathological theories, bacillary or allergic should be re-examined in the light of this new semiology. We should not overlook so important a sign of other diseases due to a filterable virus such as herpes and zona which I call lymphocytic meningitis. In particular the bacillary theory appears untenable, the meningitis perfectly curable and silence being far from the usual attacks of the Koch bacillus.

The path of transmission of this agent of a probable virus nature is itself illuminated by a new light. One should consider the infection as general (Fuchs, Muller, Marchesant, Filsenthal), and striking by way of the blood stream the particularly receptive tissues: uvea, meninges, internal ear. The way of the chiasma appears little less probable from the fact that lymphocytosis is so nearly contemporaneous with the lesions of the sympathising eye, which my first observations had not allowed me to establish.

At the same time many points are still obscure in the study of the meningeal reactions of sympathetic ophthalmitis in default of a sufficient number of examinations of the C.S.F. of patients.

It is with the object of arousing interest in these new examinations that this article has been written.

---

* Les Uveites de cause Inconnue, Bessiére et Corcelle. *Soc. d'Ophtal. du Sud Oest*, Dec. 1946.

CONJUNCTIVITIS DUE TO EXPOSURE TO DIMETHYL-SULFATE*

BY

H. J. STERN

JERUSALEM

A WORKER in a pharmaceutical laboratory presented himself complaining of bloodshot eyes which had existed for six days. He hardly felt any discomfort apart from an occasional slight itching; no lacrimation or secretion were present.

On examination both eyes were found to be bloodshot, the bulbar conjunctiva being injected only in the area exposed to the air. Neither the palpebral conjunctiva nor the bulbar conjunctiva normally covered by it showed any changes. The line of demarcation between the hyperaemic and the normal bulbar conjunctiva was rather sharply defined. The cornea was normal. Apart from the hyperaemia, the slightly oedematous conjunctiva had a peculiar opaque aspect, the superficial vessels only being clearly visible. Especially on the slit-lamp this opaqueness of the bulbar conjunctiva was striking.

A conjunctival smear did not show any organisms. A drop of adrenalin solution 1 : 1000 reduced the congestion considerably and the conjunctiva took the aspect of a opaline glass.

The clinical picture—hyperaemia and infiltration of the exposed bulbar conjunctiva—together with the information as to the occupation of the patient, suggested a chemical agent as the cause for the condition. This substance would probably be present in the atmosphere in the form of a vapour or fume; dust would be washed into the inferior fornix and exert its irritating action there, while the fornix was entirely normal.

The patient had been engaged in work entailing the use of dimethyl-sulfate, a substance which is used to introduce the methyl group into certain chemical compounds.

Dimethyl-sulfate $(CH_3)_2SO_4$, is a colourless, heavy oil which has a boiling-point of ca. 188° C. Direct application to the skin produces a very intensive reaction, and its vapours are known to have an irritative effect on the mucous membranes. Prolonged exposure to it may cause serious nervous symptoms.

The noxious effect of dimethyl-sulfate on the eyes has been subject to a number of publications at the beginning of this century.

Weber[1] was the first to recognize its toxicity and published three cases: two were workers who had been exposed to dimethyl-sulfate fumes in the course of their work; one of them died from lung

* Received for publication, April 24, 1947.

complications. The third one was a chemist who had upset a bottle of the substance on his clothes and had suffered severe burns. All three cases showed a violent conjunctivitis, the first one with necrotic patches on the palbebral conjunctiva. No corneal involvement was noted. Weber experimented on some animals and found that dimethyl-sulfate rubbed into the skin caused local burns and a mild irritation of the eyes due to the fumes. Inhalation of the fumes caused watering of the eyes after 10 minutes; after 1½ hours the conjunctiva was violently inflamed and the corneal tissue had become opaque. Ingestion of the substance did not cause any eye symptoms.

Erdmann[2] published the case of a chemist who displayed a violent conjunctivitis after having been exposed to dimethyl-sulfate fumes. While other workers had remained unaffected, he suffered from a marked reddening of the tarsal conjunctiva and a violent injection and oedema of the bulbar conjunctiva. The cornea showed some fine, greyish opacities in the area of the lid aperture. After 24 hours the cornea was opaque and the epithelium became detached in big vesicles. The condition receded slowly and the cornea became entirely clear, but with the corneal loupe some fine opacities remained visible.

The same author[3] published some more cases all of which showed irritation of the tarsal and bulbar conjunctiva; some of them displayed also corneal complications.

Adams and Cridland[4] published another case of a chemist who had started to complain of ocular symptoms some four hours after having been exposed to dimethyl-sulfate fumes and was still displaying irritable and watery eyes after three weeks when he was first seen. The ocular conjunctiva in the palpebral aperture was much injected and considerably oedematous. The palpebral conjunctiva was normal and the corneal epithelium sound, but there were some keratic precipitates present in both eyes. The patient suffered from a loss of taste and smell, and there was a doubtful contraction of the visual fields. The patient recovered entirely within three months. The authors assumed the presence of an affection of the cranial nerves because of the neurological signs.

The case published here resembles most the last one but seems to have been milder still as he presented neither the keratic precipitates nor the neurological complications of the previously quoted case. The patient was engaged in supervising a process in which dimethyl-sulfate is dropping slowly into a container in which the substance to be methylated is stirred electrically and develops a considerable temperature. The fumes of dimethyl-sulfate seem to have been responsible for the conjunctival irritation. The mildness of the symptoms and the fact that the patient did not connect his

eye condition with his occupation made the diagnosis difficult. Only the peculiar localization of the conjunctival irritation in the area of the lid aperture made it possible.

The patient was advised to stop working with dimethyl-sulfate, and the condition improved considerably. When he started after a few days to work with the substance the condition appeared again. Treatment with bland lotions and ointments failed to bring relief but bathing of the eyes with borax solution, which neutralizes the substance, improved the bloodshot appearance and itching of the eyes. Changing over to a different job brought about complete cure. It seems worth mentioning that, as in the case published by Adams and Cridland, other workers in the same laboratory who had previously done exactly the same job had never been affected.

REFERENCES

1. WEBER.—*Arch. f. Exp. Pathol. und Pharmac.*, Vol. XLVII, p. 113, 1902.
2. ERDMANN.—*Arch. f. Augenheilk.*, Vol. LXII, p. 178, 1909.
3. ——— *Arch. f. Augenheilk.*, Vol. LXIV, p. 245, 1909.
4. ADAMS AND CRIDLAND.—*Ophthalmoscope*, Vol. VIII, p. 713, 1910.

ANNOTATION

Patron Saints of the Eyes

An abridged reprint of the paper entitled as above, by Koch, is published in the Supplement to the Sight-Saving Review, 1944. The original was the author's thesis for membership of the American Ophthalmological Society and appeared in February last year. Here is given the lore of some of those saints who, in the middle ages, were canonized for miracles in connexion with sight. These saints are four in number: St. Lucy, St. Odille, St. Clair and St. Augustine of Hippo. St. Lucy was a virgin martyr of Syracuse, born c. 283 A.D. Her name was invoked principally by those suffering from external diseases of the eye. The legend of St. Odille should be familiar to those who know the Ingoldsby Legends. In this paper she is said to have been born to Adalric, Duke of Alsace and his wife. Odille was born blind c. 660 A.D. and narrowly escaped being put to death by her irate father. She is reputed to have recovered her sight during adolescence, became a nun and later the Abbess of a convent where she lived in the odour of sanctity for nearly a century. Both St. Lucy and St. Odille are commemorated on the same day, December 13th.

St. Clair, whose day is November 4, was a priest and martyr of the IXth century. He is invoked, for the most part, by those in Northern France, in cases of ophthalmia. There are other Saint

Clairs also, as well as an Italian St. Clare of Assisi, in this case, a lady.

St. Augustine was born A.D. 354. His day is on August 28 according to the Roman Martyrology and June 15 in the Russian church. He seems to have been a vicious youth both in morals and in religion; but he was converted and became Bishop of Hippo.

A well documented paper full of interest.

BOOK NOTICE

Sensory Mechanisms of the Retina. With an Appendix on Electroretinography. By RAGNAR GRANIT, M.D., Director of the Nobel Institute for Neurophysiology, Professor of Neurophysiology, The Royal Caroline Institute, Stockholm. Geoffrey Cumberlege, Oxford University Press. 1947.

An idea of the scope of this book will perhaps be best conveyed by a brief historical review (naming only protagonists) of the discoveries of the physiological processes giving rise to visual phenomena.

In 1876 Boll discovered visual purple, which was exhaustively investigated by Kühne from 1877-82. Its genesis and chemical properties were elucidated by Wald (1934-39) and Lythgoe (1937-8). In 1903 König first estimated its absorption curve and pointed out its agreement with the scotopic luminosity curve. Kühne had already proved that rhodopsin was contained only in the rods of the retina, and that visual impulses were initiated by photochemical stimuli.

In 1868 Schultze found that cones predominated in the retinae of diurnal, and rods in those of nocturnal animals; and in 1898 Parinaud attributed night blindness to deficiency in the rod mechanism. In 1904 von Kries brought forward a vast array of arguments in favour of the Duplicity Theory that the rod mechanism is responsible for vision at low intensities of light, and the cone mechanism for vision of higher intensities and for colour vision.

Du Bois Reymond's discovery of the "negative variation" in nerves (and also the resting potential of the eye) in 1849 may be regarded as the starting point of electrophysiology. Since then overwhelming evidence has accumulated that even if changes in electrical potential are not the actual cause of nerve impulses they are a quantitatively accurate reflection of the actual cause. Holmgren (1865-82) and Dewar and McKendrick (1873-7), discovered the electroretinogram (ERG); and Gotch (1903-4), with the capillary electrometer, obtained the first ERGs which embodied all the features now known to us. Valve amplification has provided instruments fast enough to follow the rapid action potentials in the nerve

from an end organ. The retina was the first sense organ to be analysed by it (Chaffee, Bovie and Hampson, *1923*). By it Adrian in 1928 proved that every sense organ reacts to an adequate stimulus by discharging a series of brief action potentials of constant size through its nerve fibre.

The ERG is a composite curve which integrates the complex electrical responses to stimulation in the retina. In this respect it differs from the comparatively simple responses in the optic nerve to the same stimulus. The typical ERG (Fig. 1) shows four chief alterations in the curve—a short negative change (*a*); a rapid

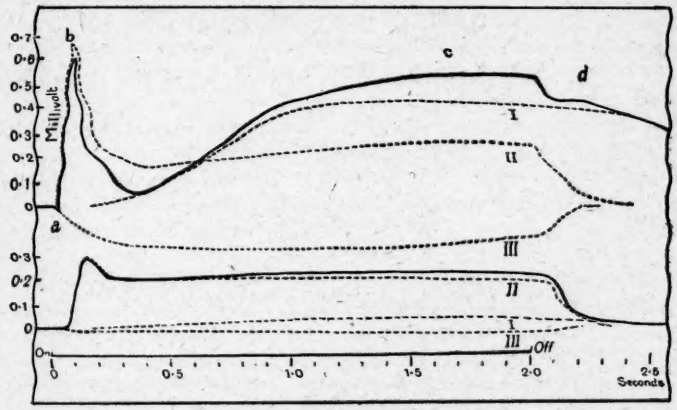

FIG. 1.

Analysis of the E—electroretinogram at two intensities—*upper*: 14 ml., *lower*: 0·14 ml.—*dotted lines*: PI, PII, and PIII.

positive wave (*b*); a slow and gradual positive wave following the fall of *b* (*c*); and an off effect, a positive change (*d*). The unexpected positive effect of the removal of the stimulus is itself evidence of the composite nature of the whole response. Granit has found two chief types of ERG: the E-retinogram in mammals (man, cat, dog, rabbit, guinea-pig, rat, mouse) (Fig. 1); and the I-retinogram in amphibia, fish, reptiles and birds (Fig. 2). The former seem to show a dominance of positive, excitatory, and the latter of negative, inhibitory components; but the responses in each are complicated by the preponderent type of retinal receptors (rods and cones), and the condition of adaptation.

The analysis of the ERGs shows that a minimum of three components suffices to explain a large number of the results obtained from various forms and conditions of stimulation; but it must be regarded as merely a first approximation. Einthoven and Jolly (1908) and Piper (1911) discussed three components, but Granit's

analysis (1933) is the most exhaustive and best established. His three component are PI, responsible for the *c* wave; PII for the *b* wave—both positive responses; and PIII for the *a* wave, negative and inhibitory.

Characteristics of the E-retina.—Ether successively eliminates PI, PII and PIII, anoxia removes PII, leaving PI and PIII; produces a negligible response at low and large at high intensities: the latent period of PIII is identical with that of the *a* wave. PI diminishes or disappears on light adaptation, and PII can be isolated by decreasing the illumination in the scotopic eye.

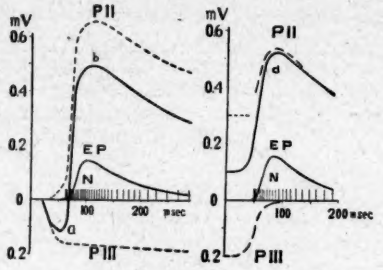

FIG. 2.

Analysis of the I–E-electroretinogram of the light adapted frog at "on" and "off"—*dotted lines*: PII and PIII (there is no PI in the light adapted frog retina); EP: electronic potential; N: nerve response; a, b, d: electroretinogram.

Characteristics of the I-retina.—PI is very slow and large in scotopia, absent in photopia: PIII and *d* wave larger in photopia. Adrenalin causes great increase in the latent period and duration of the *b* wave; it stimulates PI and increases the *d* wave. KCl in glucose eliminates PI and PII; the isolated PIII increases with increased intensity and prolonged exposure, and the optic nerve discharge is eliminated: the *a* wave is proved to be the commencement of PIII. Alcohol depresses PIII, so that it, after KCl, leaves a purely positive response. PII cannot be isolated, as in the E-retina. The large *d* wave of the photopic I-retina is due to diminution of PIII plus re-activation of PII. The initiation of both the *b* wave (PII) and the *d* appear to be due to pre-excitatory (*a* wave) and post-excitatory inhibition. The process responsible for PIII does not penetrate the optic nerve; hence the *a* wave is represented only by an inhibition of impulses, and PII is alone responsible for the electronic potential in the nerve.

PI is chiefly, if not exclusively, localised in the rod pathways, and may originate in the rods. Thus, the *c* wave is absent from pure cone eyes (turtle, tortoise, horned toad), and also in the frog with long wave-length stimulation. PIII is ontologically the oldest component (Keeler, Sutcliffe and Chaffee, 1928), and may originate in the neuroepithelium. It is most marked in cone eyes, but its potential reflects the Purkinje shift, so that it is also a feature of the rod system (Therman, 1938). Its greater development in cone retinae indicates the influence of amacrine cells. (The cones in the human retina are each supplied with a separate amacrine cell, Greeff, 1900). Its latent period diminishes with increased area of retina stimulated, suggesting that it is influenced by interaction in the

retinal synapses (Adrian and Matthews, 1925). "The whole picture of the behaviour of PIII during and after illumination suggests a piling up of inhibition during stimulation followed by its sudden destruction at "off" resulting in a release of excitation (Granit). "The complications of the retinal response at "on" and "off" are due to the intervention of pre- and post-excitatory inhibition, continuously active processes which are of extreme importance to the visual act. The discovery of the part played by inhibition in the retinal response, particularly with regard to the "off" effect, is the most important contribution that has been made by the electrophysiological method to the study of vision as a whole" (Granit).

PII is the most variable and complex response: "it represents the sum total of a number of processes with different latent periods and rates of appearance, and which produce different amounts of positive potential." Its reaction to chemical agents shows that it does not originate in the rods and cones. It probably represents the result of stimulating bipolar cells, as modified by their relationship to individual or grouped cells and cones, and their interaction with horizontal and amacrine cells. It is important to remember that some bipolar cells are connected to both rods and cones (Polyak, 1942). PII is greatly reduced by light adaptation, so that the rods are more efficient generators of it than the cones. Yet the size of the *b* wave accurately follows the scotopic and photopic luminosity curves in the dark- and light-adapted eyes of the frog, which therefore show the Purkinje shift (Granit and Wrede, 1937).

The E-retina is dominated by rods, so that the *b* wave is reduced in photopia. Yet PIII is much better developed in the cone than in the rod pathway: thus in man short wave lengths produce a typical E- retinogram (*b* wave with a small or no *a* wave) due to rods, whereas long wave lengths give a well marked *a* wave followed by a small *b* wave due to the cones (Adrian, 1945).

The I- retina is dominated by cones. In it PIII is dominant in pure cone eyes, and there is very little adaptation, though the pigeon ERG, dominated by cones, shows the Purkinje shift (Granit, 1942). In the mixed I- retina the scotopic curve shows small *a*, good *b*, appreciable *c*, and small *d* waves. PIII is characteristic of cone, PII of rod retinae. PIII is relatively greater than PII in all retinae in the photopic state. In other words the photopic eye is more inhibited than the scotopic.

"The dark adapted eye is highly sensitive and slow, like a ballistically recording galvanometer, integrating the total quantity of energy reaching it. After adaptation to light the retina is less sensitive, but very much faster and capable of differentiating between light and darkness much better than before" (Granit). In the dark adapted retina the rods must in some way be capable of damping cone activity, possibly by "occlusion" (Sherrington), the rods using

all available pathways and thereby excluding the cones. The rod system is a mechanism for integration, the cone system for differentiation (locus, changes in area and illumination intensity, discrimination). The nature of the synaptic organisation is probably more important than the character of the receptor cells.

Optic Nerve Responses. Hartline (1932) by microdissection on the retina and Granit (1939) by microelectrodes applied to the retina near the disc have succeeded in obtaining responses from single nerve fibres. These confirm the all-or-none law by giving discharges of equal size (unless the frequency at high intensity is such that each impulse falls within the refractory period of its predecessor). They also confirm the fact that increase of stimulus causes merely increased frequency of discharge. Prolonged stimulation leads to adaptation, with consequent diminution of frequency.

Hartline found three types of response in the frog: (*a*) "on" fibres—initial burst of impulses, maintained discharge, no "off" effect (20 per cent.); (*b*) "on-off" fibres—responding only at "on" and "off" (50 per cent.); (*c*) "off" fibres—responding only at "off" (30 per cent.). In the rod retina of the guinea pig Granit (1942, 1944) found 90 per cent. "on" fibres and no trace of inhibition. They have maximal sensitivity at 500$\mu\mu$ and a scotopic luminosity curve, increasing in the short wave-lengths on light adaptation, possibly due to transient orange. The maximum frequency was 100 per second. The cat has only about 20 per cent. "on" elements, but 80 per cent. "on-off." The maximum frequency may reach 400 per sec. The rod retina shows least sign of synaptic modification. The rods give rise to long trains of impulses at a low frequency, and follow changes of intensity within narrow limits. The cones provide a mechanism of differentiation capable of responding to a wide range of intensity with variations of both frequency and impulse pattern. This response occurs both at the onset and at the cessation of illumination, so that the slightest change in the stimulus situation is translated into a new type of message to the brain.

Colour Vision. The microelectric technique has fully confirmed the identity of the *scotopic* sensitivity and the visual purple absorption curve, with its maximum at 500$\mu\mu$, in a very diverse collection animals (frogs, cats, rats, guinea pig). The *photopic* curve of retinae with enough cones corresponds with the photopic luminosity curve with its maximum at 560$\mu\mu$. Granit calls these the scotopic and photopic *dominator* curves respectively.

In the light adapted eye some elements give sensitivity curves differing from the dominator curve in that they have different maxima and show humps on the curves. Exhaustive investigation has shown that these can be analysed into a finite number of curves—*modulator* curves—which together make up the dominator curve for

the animal. Such modulator curves are shown in Fig. 3. Fig. 4 shows the theoretical synthesis of the human photopic luminosity curve.

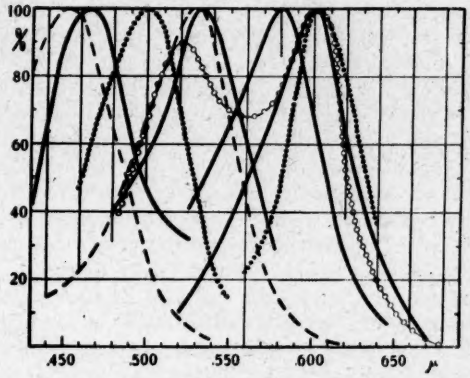

FIG. 3.

Modulator curves. *Dots*: rats; *broken lines*: guinea pig; *continuous lines*: frog; *o-o*: snake.

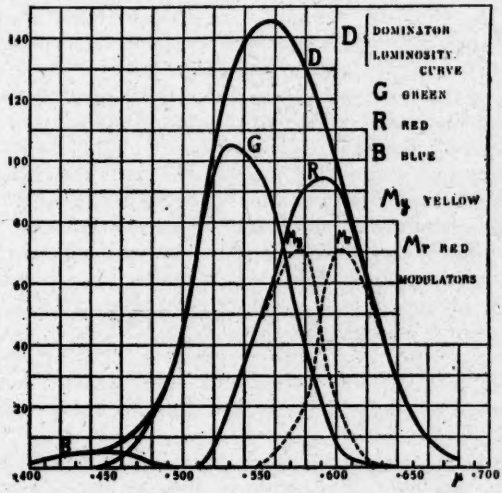

FIG. 4.

Synthesis of human photopic luminosity curve. D, luminosity curve; B, G, R, blue, green, and red fundamental sensation curves, the latter made up of two modulator curves, My and Mr.

The dominator—modulator theory shows that the scotopic and photopic curves are indeed true luminosity curves, *i.e.*, they represent

brightness differences. Both dominator reactions cover too large a part of the visible spectrum to give the higher centres any cue for colour discrimination. The modulator mechanisms are activated by light from specific central regions (440—470$\mu\mu$, 520—540$\mu\mu$, and 580—600$\mu\mu$), and thus give the higher centres their cues for colour sensations. In this respect they strongly support the trichromatic theory. On the other hand, the units of colour reception are much narrower modulator curves than the three fundamental sensation curves, which represent gross averages. Nature uses at least 6 or 7 colour mechanisms (2 red, 2 blue, and 2 or 3 green). The dominator—modulator theory affords explanations of facts which are not easily reconciled with Young's theory, *e.g.*, desaturation of the brightest parts of the spectrum, reduction of brightness on adaptation to coloured lights, summation of luminosities when two colours are mixed, the luminosity curve of deuteranopes, etc.

Hitherto our knowledge of visual phenomena has been due almost entirely to the psychological impressions derived from various forms and conditions of light stimuli, These gave little or no clue to the fundamental physiological processes involved or to their sites in the pathways from eye to brain. The first fundamental physiological fact was the discovery of visual purple and the photochemical nature of the effective stimuli. This led to the discovery of the identity of the scotopic luminosity curve with the absorption curve of visual purple and the rôle of the rods.

Granit's great contribution to the physiology of vision is the revelation of the processes in the retina and optic nerve underlying not only scotopic but also photopic vision. He has shown that the electroretinogram is the only measurable index of what takes place in the retina in response to changes in illumination. He has further elucidated the enormous importance of the synapses in the retina in both the scotopic and photopic pathways, which as elsewhere may be of a chemical nature. It must be a matter of satisfaction to him, as a disciple of Sherrington, to have been able to bring forward so much evidence of summation, facilitation, inhibition, occlusion, and so on in the retina, thus confirming physiologically its nature as a part of the central nervous system. His researches are of outstanding value not only to physiological optics but also to neurology in general.

As already mentioned his work necessitates modification of the trichromatic theory. The same applies to the duplicity theory. The "ideal" rod, to use his term, still survives as the scotopic receptor: but there are probably cone-like rods which are light resistant and are capable of mediating responses in the photopic state, probably by means of a modified visual purple.

It has always been difficult to understand how the relatively simple impulses of the optic nerve can convey to the brain the

qualitative differences of vision, and it has been customary to refer these to "higher centres." But, as Granit says, "whatever the sensation under consideration, whether flicker, colour, or brightness, the higher centres are no magicians capable of taking rabbits out of an empty hat." The complex fundamentals have been proved to have their origin in the retina. Differences of frequency and pattern provide qualitative differences in the optic nerve impulses: and it may be that, since there is a difference between the action potentials of fibres of different diameter (Gasser and Erlanger, 1924), the modulator paths may be made up of fibres of fixed size.

J.H.P.

CORRESPONDENCE

MYOPIA AND PSEUDO-MYOPIA

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—I apologize for not having answered Mr. F. S. Lavery's letter in the February number of the *Brit. Jl. Ophthal.* before.

The boy he mentions had appealed and was re-examined, and was rejected a second time before I saw him. I fear that he has misunderstood me, for I did not wish to imply that it would be in the boy's interest that he should be accepted now. I agree that it is possible that he may later become myopic, but I merely quoted his case as the starting point of my interest in this condition.

Personally, I consider that it is wiser for such cases to wait, and if, when they have reached the suitable age, their vision, etc., is satisfactory, they should avail themselves of the "Public Schools" entry facilities.

Yours faithfully,

J. P. SPENCER WALKER.

3, SELBORNE ROAD,
HOVE 3, SUSSEX.
April 24, 1947.

NOTES

Contact Lens Society A scientific meeting of the Contact Lens Society was held on April 21, at 65, Brook Street, with Professor Ida Mann in the chair. About 160 members were present. A discussion on the training of contact lens practitioners was opened by Mr. Williamson-Noble, followed by Mr. K. Clifford Hall, F.S.M.C., Mr. Frank Dickinson, F.B.O.A. (Hons.), and Mr. D. W. A. Mitchell, F.B.O.A. (Hons.), F.S.M.C., D.Orth. Others who contributed to the discussion were Messrs. G. D. McKellen, Professor Ida Mann, C. L. G. Jenkin, Dr. Minton, A. E. Hogg, L. Crawford, R. A. Jones, and A. J. Forknall.

A vote of thanks to the speakers was proposed by Mr. L. Evershed Martin and seconded by Mr. C. L. G. Jenkin.

During the course of the evening three films were shown: Mr. Davis Keeler's which showed particularly the manufacturing side; the Feinbloom film which had just been flown from the United States and was shown in this country for the first time; and the London Refraction Hospital film.

* * * *

Ophthalmology in South Africa PROFESSOR H. WEVE, of Utrecht, is in Johannesburg at the time of writing. He will lecture before the Ophthalmological Society of South Africa and will also visit Cape Town and Durban.

Dr. J. Graham Scott, late of Glasgow, has started practice in Johannesburg and has been appointed Part-time Ophthalmologist to the Mines Benefit Society. Basil Graves has also been in South Africa and is now at George, Cape Province.

* * * *

Corrigendum DR. P. H. BEATTIE'S appointment, noted on p. 320, should have read Assistant Ophthalmic Surgeon.